SPECIAL TIME EDITION

Diabetes

From Diagnosis to Empowerment

How Diabetes Affects Your Health

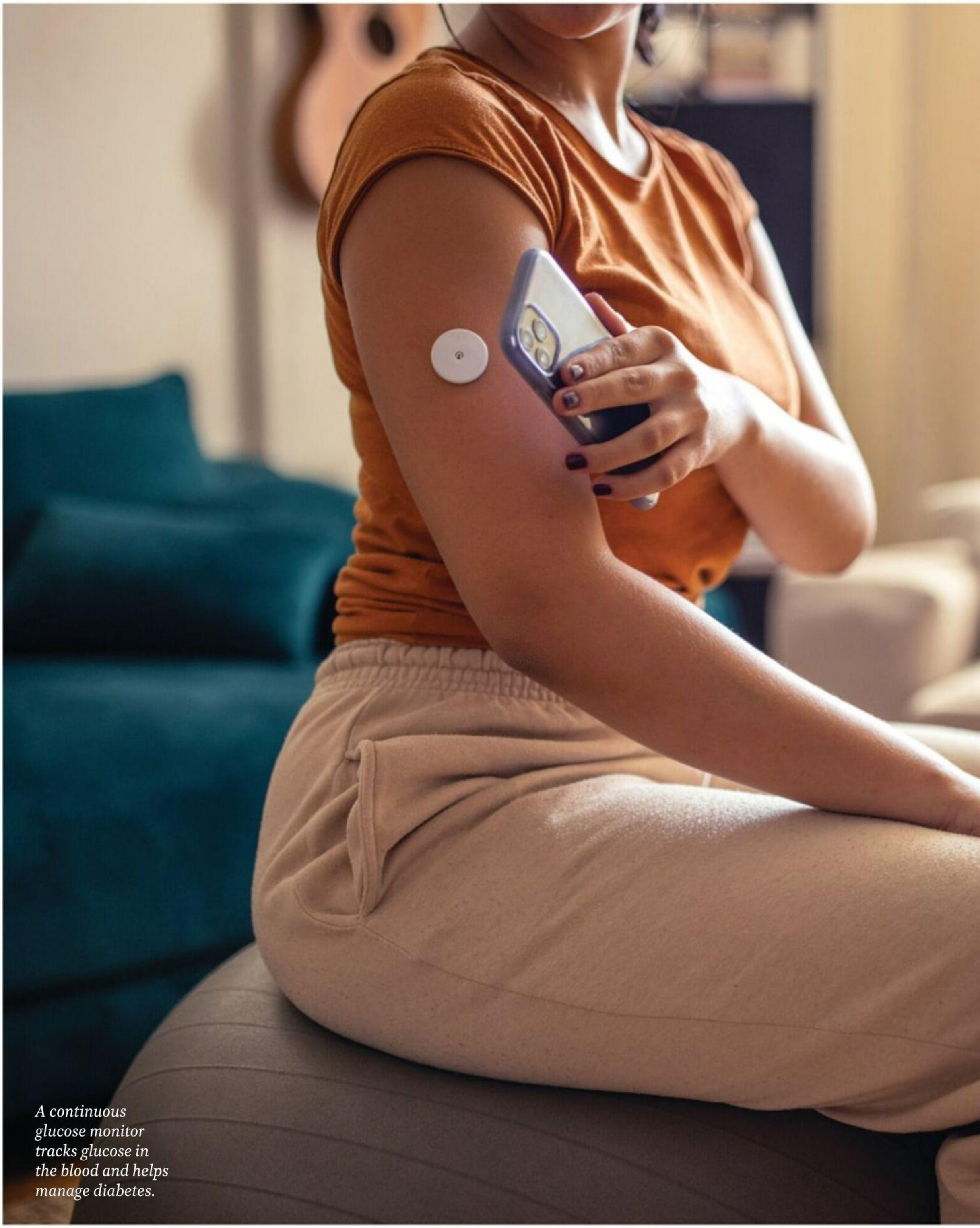
The Newest Technologies and Treatments

Strategies for Blood Sugar

LOWER CHOLESTEROL NATURALLY

SPECIAL TIME EDITION

DIABETES



A continuous glucose monitor tracks glucose in the blood and helps manage diabetes.

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MOVING TOWARD HOPE

BETTER SCREENING TECHNIQUES, ADVANCEMENTS IN BLOOD SUGAR MONITORING, AND NEW TREATMENTS ARE HELPING PEOPLE WITH DIABETES MANAGE IT BETTER.

BY MARKHAM HEID

THE SYMPTOM—EXCESSIVE URINATION—was distinct, and the treatment, experimental: a regimen of elderberry, milk, green dates, and "water from the bird pond." It was the Third Dynasty in Egypt, the patient was the Pharaoh Djoser, and the doctor, Hesy Ra, the ruler's chief physician. There's no record of whether Djoser's condition improved, but today, more than 4,500 years later, his disease would receive a diagnosis familiar to many: type 2 diabetes.

Medicine has come a long way since those pond water days, which is fortunate, because the demand for effective diabetes treatments has never been so great. Around the world, 529 million people are living with the disease. More than 1 in 10 Americans now have diabetes, according to CDC estimates. An additional 38 percent of Americans have prediabetes, which means their blood glucose levels are concerningly elevated, placing them at high risk for developing type 2 diabetes. These figures are expected to rise even higher in the coming decades.

"The average American has a 30 percent or greater chance of developing diabetes, and the lifetime risks of disabling complications are greatest among children and young adults who develop diabetes," says Dr. John Buse, distinguished professor of medicine and director of the Diabetes Care Center, at the University of North Carolina. "So it's a huge problem, especially among communities of color and people with social and economic barriers." To his point, researchers have found that the prevalence of diabetes is higher among Black and Hispanic individuals compared to their White counterparts, and also higher in people who live in rural environments, as opposed to urban environments.

While the effects of the disease on the American populace and health care system continue to worsen, medical science's ability to treat the condition is improving. The last century saw steady advancements in doctors' ability to treat diabetes, and the past decade has welcomed the emergence of two new classes of drugs that many experts are hailing as generational advances.

The first of those new drugs are the glucagon-like peptide-1 (or GLP-1) agonists. These include weight-loss drugs such as semaglutide (brand names include Ozempic and Wegovy), and they work by mimicking the action of a glucose-lowering hormone called GLP-1. The second class of breakthrough drug is a sodium-glucose cotransporter-2 (SGLT-2) inhibitor. These drugs block the activity of a specific protein, which effectively reduces

Two new classes of drugs, GLP-1 agonists and SGLT-2 inhibitors, have been hailed as generational advances for the treatment of diabetes.

the amount of glucose in the blood and kidneys. "Each of these drugs independently is associated with meaningful benefits, and many people in the field believe that if money wasn't an issue and these drugs were inexpensive, arguably just about everybody with type 2 diabetes would be treated with both," Buse says.

Time and follow-up research are needed to confirm if these drugs, either alone or in combination, are the durable solution to diabetes they appear to be. Time will also help bring the cost of these drugs down and perhaps make them simpler to administer. Right now, for example, most GLP-1 drugs are given as a weekly or daily injection. But there's active research into the development of an oral GLP-1 tablet.

Alongside the latest drugs, new advancements in blood-sugar monitoring are also helping people with diabetes better control the condition and reduce risks. These include continuous glucose monitoring (CGM) sensors—small patches attached to the skin that record a person's blood sugar levels every few minutes. "These sensors include a transmitter that can send the glucose value wirelessly to a smartphone app, so the patient and their health care provider can see how their values are changing," says Dr. Roy Beck, medical director of the nonprofit Jaeb Center for Health Research, in Florida.

Researchers are also investigating new methods of administering insulin in hopes of better controlling the blood-sugar swings that lead to the symptoms and complications of diabetes. These include so-called automated insulin delivery systems—clusters of interconnected technologies that can monitor blood sugar and also administer insulin as needed, without a patient having to do anything themselves. "If you're able to achieve good blood sugar levels, your risk of having any complications is basically zero," Buse says.

Apart from medical treatments for type 2 diabetes, experts say improved screening techniques and a greater understanding of the disease have also improved our ability to treat or prevent the condition with lifestyle changes. There's evidence that avoiding processed foods, getting regular exercise, and managing stress may all provide benefits in reducing the burden of type 2 diabetes.

To be sure, there's more work to be done. The data on diabetes prevalence, both in the U.S. and abroad, are stark. And while nothing we have today could be called a cure, we have never been so well-equipped to combat the disease. There are challenges ahead, but also reason for hope. ☐

CHAPTER 1

UNDERSTANDING DIABETES

FOR DIABETES TYPE 1 AND TYPE 2, SYMPTOMS ARE SIMILAR, BUT THE CONDITIONS HAVE DIFFERENT CAUSES AND TREATMENTS.

EXPLAINING TYPE 2 DIABETES

THE DISEASE RESULTS FROM HIGH BLOOD SUGAR AND IS AT EPIDEMIC LEVELS. THE GOOD NEWS: OUR UNDERSTANDING OF THE CONDITION IS STRONGER THAN EVER, AS IS OUR ABILITY TO MANAGE IT.

BY MARKHAM HEID

IN THE FIFTH CENTURY BCE, A SURGEON in India described a patient's honey-like urine, which was so sugary that it attracted ants. A few hundred years later, a physician in ancient China treated a person with a curious ailment that caused excessive thirst, frequent urination, and unexplained weight loss.

These historical accounts are now cited as evidence that diabetes has been with us for thousands of years. Experts who study and treat the disease today say the early symptoms of type 2 diabetes would have been familiar to their predecessors of antiquity.

"Increased urination, increased thirst, and unexplained weight loss are some of the first symptoms patients notice when their blood sugar levels are significantly elevated," says Dr. Francisco Pasquel, a diabetes specialist and associate professor of endocrinology at Emory University, in Atlanta.

While type 2 diabetes was once rare—occurring mostly in those with more wealth—the condition is now so commonplace that it has been referred to as the largest epidemic in human history. Around the world, more than half a billion people are living with diabetes. That figure includes the nearly 40 million Americans who have the condition. And while type 2 diabetes traditionally emerges during adulthood, the last two decades have seen a concerning spike in diagnoses among children. By some estimates, 1 in 4 adolescents has prediabetes, meaning their blood sugar levels are elevated enough to place them at high risk for developing type 2 diabetes.

"These numbers are pretty shocking," says Dr. Sun Kim, a diabetes treatment specialist and associate professor of medicine at Stanford University. "The reasons why diabetes is so common are severalfold, but I think in general you could say we're genetically predisposed to diabetes, and the lifestyles and environments today create kind of a perfect storm for bringing out that risk."

That's the bad news. The good news is that medical science's understanding of the condition has never been stronger, nor the ability to manage and treat the condition.

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WHAT IS TYPE 2 DIABETES?

Type 2 diabetes is a disease of excess blood sugar, also called high blood glucose or hyperglycemia.

Glucose is one of the body's main sources of energy, and it's carried throughout the body via the blood. The amount of glucose in a person's blood is regulated by a hormone called insulin. When blood sugar levels are elevated, the pancreas releases insulin into the bloodstream. Insulin causes the liver, muscle, and fat cells to absorb excess glucose. But in people with type 2 diabetes, this tight regulation of blood glucose goes awry. "The glucose can't get into the cells, and the most common reason for this is a resistance to the action of insulin," Pasquel explains.

The kidneys are responsible for cleaning and filtering blood. When overwhelmed with too much blood glucose, the kidneys end up dumping that excess glucose out of the body via urine. Glucose carries water with it, and this explains why frequent urination, thirst, and weight loss are some of the earliest detectable symptoms of type 2 diabetes. Blurry vision is another noteworthy early symptom, and it's caused by swelling of the lens of the eye due to excess blood sugar.

Too much blood sugar also causes progressive harm to the body's vasculature, which is the network of major and minor blood-carrying vessels that run throughout the body. The repercussions of this harm are numerous: Heart disease, arterial disease, nerve pain, and vision loss are all consequences of type 2 diabetes. If not properly managed, the condition can eventually lead to heart attacks, heart failure, stroke, blindness, kidney disease, limb amputation, and other potentially deadly complications, Pasquel says.

While the first symptoms of type 2 diabetes are somewhat predictable, he warns that type 2 can be present and causing damage long before these symptoms show up. "One part of this disease that is unfortunate is that it may be silent, meaning patients have this disease without having symptoms, or the symptoms are so subtle that they don't lead them to seek medical attention," he says. "If you wait until symptoms emerge to start treatment, the average person would have had the disease already for between five and 10 years."

What causes type 2 diabetes? It's a simple question with a complicated answer.

"It's hard to pull out a single cause, but everyone in the field agrees excess weight due to increased body fat leads to this cascade of issues that can lead to insulin resistance," Kim says.

Adipose tissue (fat) is associated with immune and molecular alterations that are thought to drive insulin resistance. "In people with type 2 diabetes, we see fat accumulating in places it's not supposed to be—the liver and heart and muscles," Pasquel says. "We see a chronic inflammatory state in these fat cells, where they are basically producing these adipocytokines and hormones that cause insulin resistance." He also says that diabetes is associated with "several other defects" that may promote hyperglycemia, including alterations in the production of some gut hormones that are important for metabolism, and also increased reabsorption of glucose in the kidneys.

"We also see that when people lose weight, a lot of this is reversed, so that's why there's so much focus on weight," Kim adds.

DIAGNOSIS AND TREATMENT

Because type 2 diabetes can be present and doing damage long before symptoms arise, screening is vital. Since 2021, the U.S. Preventive Services Task Force—a government agency responsible for guiding health policy in order to prevent disease and extend life—has recommended diabetes screening for all adults ages 35 to 70 who have excess weight or obesity, regardless of whether they have symptoms of diabetes. (The agency does not recommend screening in asymptomatic younger people.)

Screening for type 2 diabetes is essentially the same process a health care provider would follow to diagnose a symptomatic person. It often involves a fasting plasma glucose test, an oral glucose tolerance test, and a hemoglobin A1c (HbA1c) test. The fasting plasma glucose test measures the amount of glucose in a person's blood after a period without food. The glucose tolerance test measures the levels of glucose in the blood two hours after drinking a syrupy solution containing 75 grams of sugar, Pasquel explains. The hemoglobin A1c test measures blood glucose outside of these fasted or challenged states.

Once someone is diagnosed with type 2 diabetes, treatment can vary from person to person, depending on the severity of the disease, but it often involves both medication and lifestyle changes. "Until recently, a patient would typically always have metformin as the first drug," Pasquel says. Metformin

Research has demonstrated that injectable semaglutides such as Wegovy are effective over the long term for blood sugar control in people with type 2 diabetes.

works by reducing the liver's production of glucose, and it can also improve insulin sensitivity and reduce the amount of glucose absorbed in the gut. While metformin is still prescribed for some people with type 2 diabetes, Pasquel says newer medications have led to a "paradigm shift" in the treatment of the disease. "The newest GLP-1 drugs are much more potent than metformin and have additional benefits on weight and cardio protection," he says.

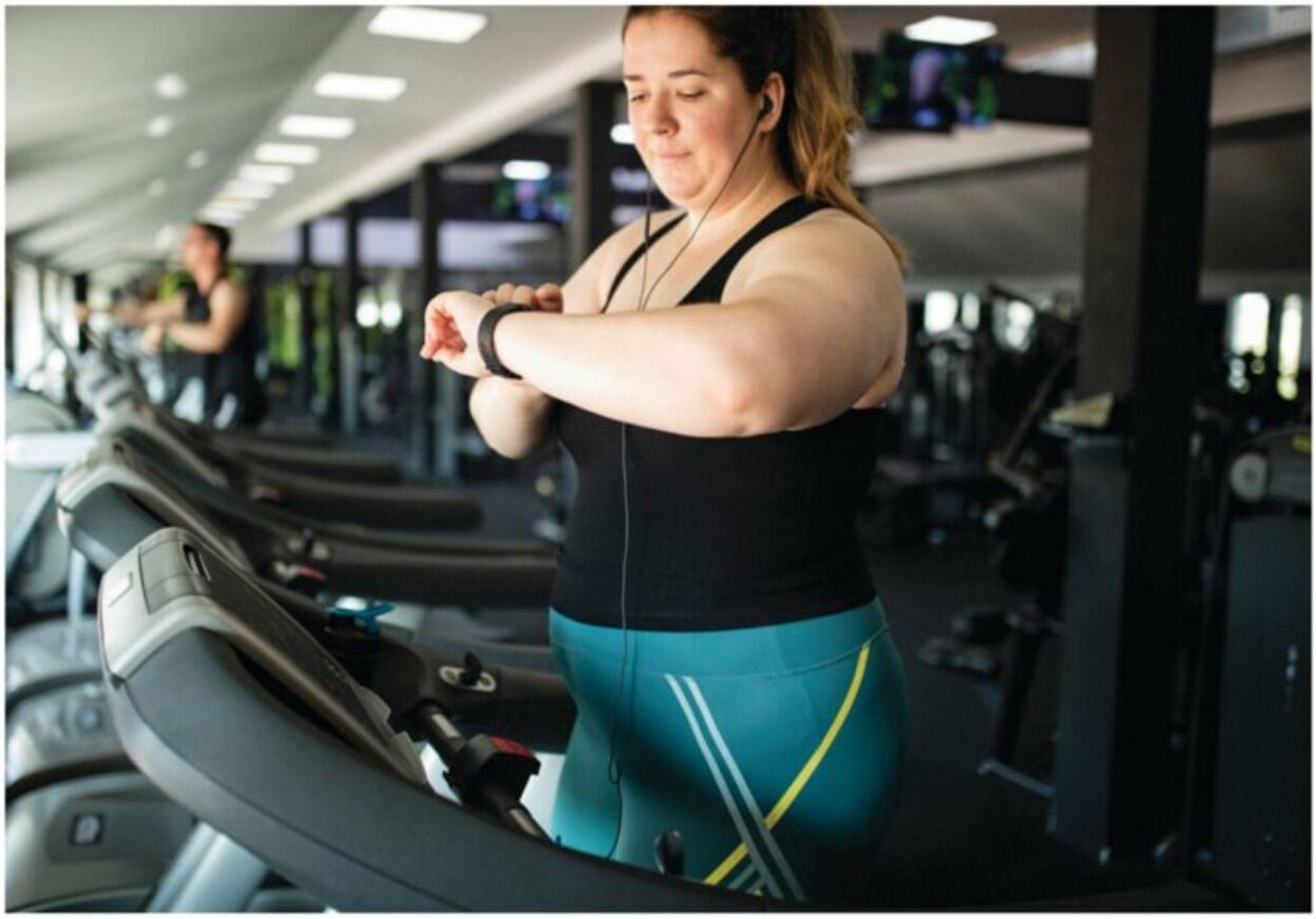
Glucagon-like peptide-1 (GLP-1) agonists have been around for more than a decade. But Pasquel says the latest versions of these drugs, including semaglutide (with the brand names Ozempic and Wegovy) and tirzepatide (Mounjaro and Zepbound), can lower a patient's blood sugar levels to the point where they technically no longer have diabetes. "If you stop the medication, there is rebound," he says. "So it's not really a cure, but they can prevent many of the complications of high blood sugar."

These GLP-1 medications are so new that a lot of the long-term health effects are not well mapped, including the impact on people who take them off-label to aid in weight loss. Still, experts say these drugs have changed the treatment landscape for people with diabetes, and they believe newer and better drugs are in the offing.

A PATIENT'S ROLE

While the latest medications appear to be a major advancement in the treatment of type 2 diabetes, experts say a lot still depends on the choices and lifestyle of the patient.

First and foremost, they say it's necessary for people to take medications as directed and not abandon the therapy, which is not uncommon. The biggest deterrent is cost. Many of the newest medications are expensive, and securing insurance reimbursement can be tricky. "A big issue is related to the mayhem of the U.S. insurance industry," says Dr. John Buse, distinguished professor of medicine and director of the Diabetes Care Center, at the University of North Carolina. "Almost every year, these pharmacy benefits management companies flip from drug A being preferred to drug B,



and this can make things difficult and complicated for patients."

Some people just don't like taking a drug, and they stop once they've lost weight or gotten their blood sugar under control. "A lot of people see diabetes as a lifestyle problem, and they decide they'll just work on that and they don't need medications," Kim says. "In an ideal world, yes, many people could manage diabetes with lifestyle, but the truth is that we need additional tools, including medications."

Lifestyle choices, in fact, matter equally. People with diabetes need to exercise regularly and eat healthfully, both limiting processed foods and added sugars and eating three different vegetables and two different fruits a day, Kim says. "There are so many crazy diets now, so I think people get confused and they say, forget it, I'll just eat what I want," Kim says. Two other valuable pieces of advice: Get a good night's sleep and learn to manage your stress.

Experts say some newer monitoring technologies can help people with type 2 manage the condition. These devices include wearable app-connected patches that continually measure blood glucose, offering patients and their providers insights into how diet and activity are affecting blood sugar.

While these tools can be helpful—and life-saving—they also come with some downsides. "Some of these continuous glucose monitors give you readouts every five minutes, seven days a week, and you see some people who almost become obsessively engaged with their blood sugar and their efforts to make it perfect all the time," Buse says. "People beat themselves up over every misstep, but the truth is, good control of diabetes doesn't require total perfection."

Exercise not only helps people with type 2 diabetes strengthen muscles and bones, it helps their bodies to use insulin, which controls blood sugar.

SOLVING DIABETES

While the prevalence and costs of type 2 diabetes are expected to rise in the coming years, experts say our ability to manage and treat the disease has never been stronger, and they expect that further advancements are just around the bend. "The serious complications of the disease are now essentially 100 percent preventable with intensive intervention," Buse says. In most cases, he adds, "we can now achieve outstanding control of diabetes, and people can expect a normal lifespan without complications." □

PREDIABETES: A PRIMER

WHEN BLOOD SUGAR IS HIGH, BUT NOT HIGH ENOUGH TO BE CONSIDERED CLINICAL TYPE 2.

BY ASHLEY ABRAMSON

One of the dangers of type 2 diabetes is that it can develop quietly over a number of years, without obvious symptoms, as glucose levels rise and the body develops a resistance to insulin. This phase is known as prediabetes and often is discovered by accident, during routine medical work, when blood sugar levels register higher than normal, says Philip Orlander, MD, professor and endocrinologist with UTHealth Houston. You can also be tested specifically for prediabetes.

A precursor to type 2, prediabetes has many of the same root causes as type 2, including excess weight, age (being older than 45); physical inactivity (exercising less than three times a week); having given birth to a baby who weighed more than 9 pounds; and having close family members who have type 2 diabetes. Race and ethnicity also play a role in prediabetes, with African American, Hispanic/Latino American, American Indian, Alaska Native, Pacific Islander, and some Asian American people at higher risk for the condition.

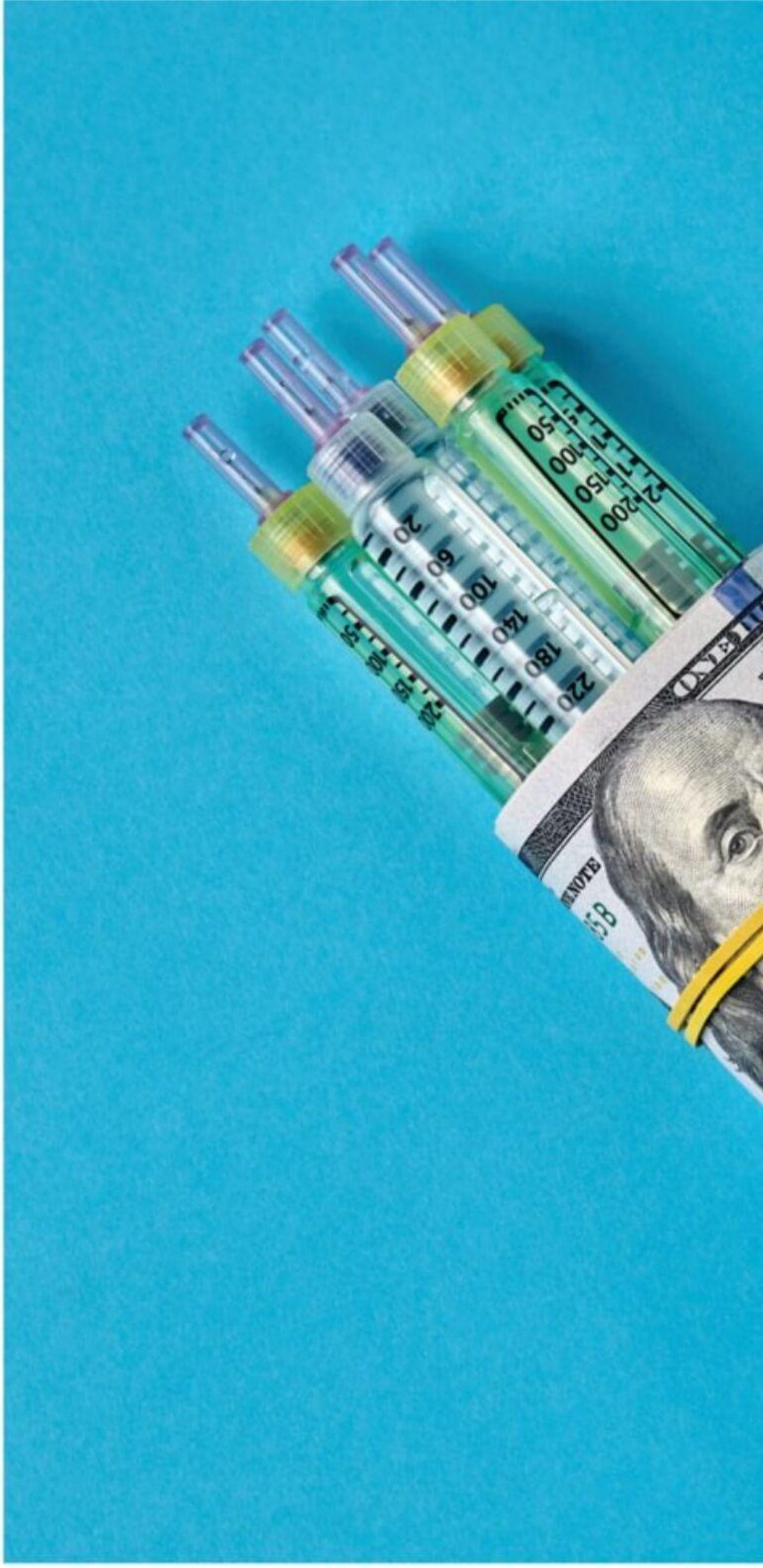
Prediabetes is a serious health condition that can increase the likelihood of diseases associated with type 2, such as cardiovascular disease, stroke, and kidney, eye, and nerve damage.

However, not everyone with prediabetes will develop type 2 diabetes, Orlander says, especially if the person with the condition continues with medical attention and makes lifestyle changes. A healthy diet, coupled with at least 150 minutes of physical activity weekly, can help restore healthy blood sugar levels and prevent type 2 diabetes. Losing even 5 percent to 7 percent of your body weight can reduce your risk of developing type 2 diabetes.

THE HIGH COST OF DIABETES

CAPS ON INSULIN PRICES ARE A WELCOME DEVELOPMENT, BUT PATIENTS ALSO FACE THE COSTS OF MEDICAL VISITS, SPECIAL DIETS, AND GLUCOSE-MONITORING DEVICES.

BY HALEY WEISS



EARLY EACH YEAR, KRISTIN THOMPSON-Lerberg sits down with her husband to plan how they will reach the $3,000 deductible for their family's insurance policy. The conversation historically was short: Thompson-Lerberg needs about eight vials of insulin each month to treat her type-1 diabetes, and at $275 per vial before insurance kicks in, it took just two months to reach the deductible with insulin alone.

But the Thompson-Lerberg's budget expanded in March 2023 after pharmaceutical giant Eli Lilly announced that the monthly out-of-pocket prices of their insulin brands would soon be capped at $35, regardless of a person's insurance. For Humalog, the company's best-selling insulin brand (and the one Thompson-Lerberg uses), the change amounted to a 70 percent cut in list price. The news from Eli Lilly was "life-changing for our family," Thompson-Lerberg says.

While some criticized Lilly's announcement as being too little, too late, after decades of insulin price hikes, the reduction had a huge financial impact for many of the 8.4 million Americans who rely on insulin to regulate glucose levels. Diabetes care accounts for a quarter of all money spent on U.S. health care, according to the American Diabetes Association, and insulin is a large part of that price tag. A quarter of people in the U.S. with diabetes have reported rationing their insulin for financial

reasons. "Diabetes is a very expensive illness," says Serena Valentine, executive director of the health and wellness nonprofit CORE Initiative in Houston, who has type-1 diabetes.

Valentine remembers being evicted, as a student, from her apartment nearly 20 years ago because she had to funnel her rent toward insulin payments. "It wasn't really a choice," she says. "While I lost an apartment, some people lost their lives."

The high cost of the drug has long kept diabetes patients and advocates focused on how to get or improve access to insulin. With the price cap comes a chance to redirect their efforts and energy toward other challenging—and expensive—aspects of the disease.

Making insulin more affordable is only the first step in addressing obstacles to diabetes management, Valentine says. Other expenses of care include regular trips to the doctor and managing the right diet to keep glucose levels stable. "You should be able to readily access the guidance of the people that you need to talk to without finances being a barrier," says Thompson-Lerberg.

For many patients, the money saved on insulin has gone toward managing their diabetes in other ways. Thompson-Lerberg recently switched from a standard insulin pump to a continuous glucose monitor, a device that measures her glucose levels every five minutes and automatically delivers targeted amounts of insulin to keep her within a safe range—"almost like having an external pancreas," she says. It's the gold standard for diabetes management. But until the insulin price cut was announced, she hadn't planned to use one around the clock.

Continuous glucose monitors are pricey, even beyond the initial cost of the devices themselves; the wearable sensors that the machines require can carry a price tag of more than $200 per month. Now, however, "not having to pay so much for insulin absolutely frees up a little more funding to be able to use it," she says.

Thompson-Lerberg is hopeful that cheaper insulin prices will give more people with diabetes access to disease-improving solutions like these—and that this, in turn, will help lower the stigma that she and others she knows have faced from specialists who don't appreciate the everyday challenges of diabetes management. "I've had times where I was shamed for having high blood sugar," she says. "When people have access to what they need and can more independently self-manage, then I think people are more willing to ask for help."

Jessyka McCaulley, a 30-year-old entrepreneur who has type-1 diabetes and sells diabetes-awareness merchandise online, says that the money she saves on insulin will go right back into her small business and platform, "just to help spread awareness that is still so much needed."

"Diabetes is definitely a mental disease as well as a physical one," she says. "This is one less stress that we have to worry about." □

HOW THE MICROBIOME MIGHT PREDICT DIABETES

STUDIES OF THE MICROBIOME ARE HELPING US UNDERSTAND INSULIN RESISTANCE, AND A ROUTINE SCREENING OF IT FOR DIABETES IS EXPECTED TO BECOME A ROUTINE PART OF HEALTH CHECKUPS.

BY ALICE PARK

A GROWING BODY OF RESEARCH IS finding links between how diet, weight, and environmental exposures, among other things, can affect the mix of bacteria that make up our microbiomes. There are still no clear guidelines for specific microbial combinations that could help avoid or treat disease, but the latest studies bring us closer to developing them.

Starting in 2009, the U.S. National Institutes of Health invested $170 million to better understand the universe of bacteria that live within us—the so-called microbiome. In the first phase of the project, researchers focused on cataloging the myriad types of microbes found throughout the body, including in the mouth, nose, gut, and reproductive tract. The second phase of the research, described in three papers published in May 2019 in *Nature* and *Nature Medicine*, focused on better understanding how changes in those microbial populations affect three conditions: diabetes, preterm birth, and inflammatory bowel diseases.

THE MICROBIOME AND DIABETES

In the study on diabetes, published in *Nature* and led by Michael Snyder, director of the center for genomics and personalized medicine at the Stanford University School of Medicine, a team of researchers followed 106 people for nearly four years, profiling their microbiomes every three months using nasal swabs, stool samples, and blood tests.

The volunteers came in for extra visits when they caught a cold or the flu, and, at their will, during stressful events, such as job changes, weight gain, or travel, or any other time they thought they might have been exposed to environmental elements that could affect their health. That way, the researchers could track how these experiences impacted their immune systems and the composition of microbes in their bodies. "This cohort is probably the best studied group of people on the planet," said Snyder.

Snyder and his team found that there is no true "normal" when it comes to the microbiome. "Everybody's healthy baseline is different," he said. That said, there were some commonalities in the microbiomes of people with certain disease states, including insulin resistance.

Diabetes often starts as insulin resistance, when people become less sensitive to the effects of the hormone and start to have trouble breaking down sugar and other carbohydrates. Insulin resistance can lead to prediabetes, and 70 percent of people with prediabetes go on to develop type 2 diabetes during their lifetimes. Snyder's team found that people with insulin resistance tend to have differ-

ent microbes, which then cause immune cells to act in different ways, compared to people who are more sensitive to insulin. So when those who are insulin resistant or prediabetic get sick, their immune responses are often weaker than those who are not.

"We can predict an insulin resistance signature from the microbiome," Snyder said. Currently, detecting insulin resistance requires a six-hour test that costs thousands of dollars, but a microbial analysis, from stool samples, could cost a fraction of that.

Snyder cofounded a company to develop such a test for prediabetes, and he anticipates that regular screening of people's microbiomes for diabetes will become a routine part of a health checkup in coming years. "Having an assay for insulin resistance could be very, very powerful in catching people who might develop diabetes much earlier," Snyder said. "That's important, because managing prediabetes before it becomes diabetes is critical, since it's hard to reverse once diabetes occurs."

THE MICROBIOME AND PREMATURE BIRTH

Using the microbiome may also prove useful in predicting which women might be at higher risk of delivering prematurely. In another study, this one published in *Nature Medicine*, researchers led by Gregory Buck, director of the center for microbiome engineering and data analysis at Virginia Commonwealth University, identified microbial profiles in the vagina that were linked to higher rates of preterm birth. They found that women who delivered early, at less than 37 weeks, were less likely to have *Lactobacillus crispatus*, which previous studies linked to a healthy reproductive tract, and more likely to have a diverse community of vaginal microbes, often including four specific taxa.

When the researchers created a prediction model incorporating this information they were able to improve prediction of premature birth by up to 7 percent over current methods. "This gives us hope that we are going to be able to characterize vaginal types . . . that will provide some predictive value when it comes to preterm birth," said Buck. "Our results have generated a plethora of hypotheses that we need to now explore and prove or disprove." Other recent studies have hinted, for example, that understanding the vaginal microbiome might also help to predict in vitro fertilization success, and this latest data leads researchers to ask more detailed questions about what microbiome profile would be best for a healthy pregnancy.

THE MICROBIOME AND INFLAMMATORY BOWEL DISEASE

In the third paper, published in *Nature*, Curtis Huttenhower, professor of computational biology at the Harvard T.H. Chan School of Public Health, and his team followed 132 people for a year, some with inflammatory bowel disease and others without. They collected stool, biopsy, and blood samples in order to track whether and how their microbiomes changed during disease flare-ups and during recovery periods.

They were indeed able to identify changes in the types of bacteria that become active during flare-ups, compared to during recovery periods, as well as changes in how those microbes were impacting the immune system. So far, the study authors wrote, this isn't enough to develop, say, a diagnostic test that could predict flare-ups based on a person's microbiome, but they hope this early work might make that possible. "We can now see which microbes change in coordination with which chemicals, and how the immune system responds, and how these responses differ from person to person over time," says Huttenhower.

APPLYING THE MICROBIOME FINDINGS IN THE REAL WORLD

All of the studies continued to build the list of key players in the microbiome, which include not just the specific microbes involved but also the other factors—such as immune cells and other metabolic chemicals—that interact with the microbes to affect human health. "There has been a substantial effort to get the catalogue and the basics laid out. And we're moving on from there to understand how the parts fit together," says Huttenhower. "I imagine it will take several more years to learn how to fix those parts and make the machine work again."

One of the challenges in finding useful applications for the microbiome is how variable microbiomes can be, both from person to person and in any given individual over time. Huttenhower noted that these early studies have enabled them to "see many different ways across individual patients that the gut microbiome becomes [perturbed] and often restores itself over time." The goal, then, is to "start to put together all [the] different ways in which that can happen, and understand what is common about them."

While microbiome tests for predicting diabetes or preterm birth aren't ready for use in the clinic just yet, said Snyder, they are on the horizon. "We are learning a ton," he said. □

YOUR MICROBIOME ON MEDS

BY ALICE PARK

A NEW ORAL DRUG CAN HELP KEEP DISEASE-CAUSING BACTERIA IN YOUR GUT AT BAY.

Probiotics have long been star ingredients in dairy foods, drinks, and supplements, promising to generate a better bacterial balance to our guts.

In 2023, the U.S. Food and Drug Administration took a step toward formalizing the idea of adjusting gut-bacteria populations when it approved the first oral drug designed to treat the microbiome. First called SER-109, and now VOWST, the pill is a cocktail of bacteria that can prevent recurring infections of *C. difficile* bacteria in people who have had previous episodes and help them maintain healthy levels of gut bacteria. Keeping beneficial bacteria in proper balance could be an important way to keep disease-causing ones like *C. difficile* at bay.

The FDA based its decision on clinical trials that the drug's maker, Seres Therapeutics, conducted in collaboration with Nestle Health Science in nearly 200 people who had experienced recurring *C. diff* infections. These infections spread easily in hospitals and are challenging to treat, since many of the bacteria are now resistant to antibiotics. According to the U.S. Centers for Disease Control and Prevention, about one in six people who have had a *C. difficile* infection will have another one in two to eight weeks.

In studies on which the approval was based, people took four capsules of SER-109 daily by mouth for three days to try to prevent recurrence of the infections. Eighty-eight percent of the participants did not have another infection eight weeks after a single course of treatment—the time period during which many infections return—compared to 60 percent of those who received a placebo. Six months later, 79 percent of those who took SER-109 remained free of reinfection, while only 53 percent getting a placebo did. The pills are given after patients finish a course of antibiotics to first kill as many of the *C. diff* bacteria as possible; the microbiotic therapy then helps to restore the beneficial bacteria.

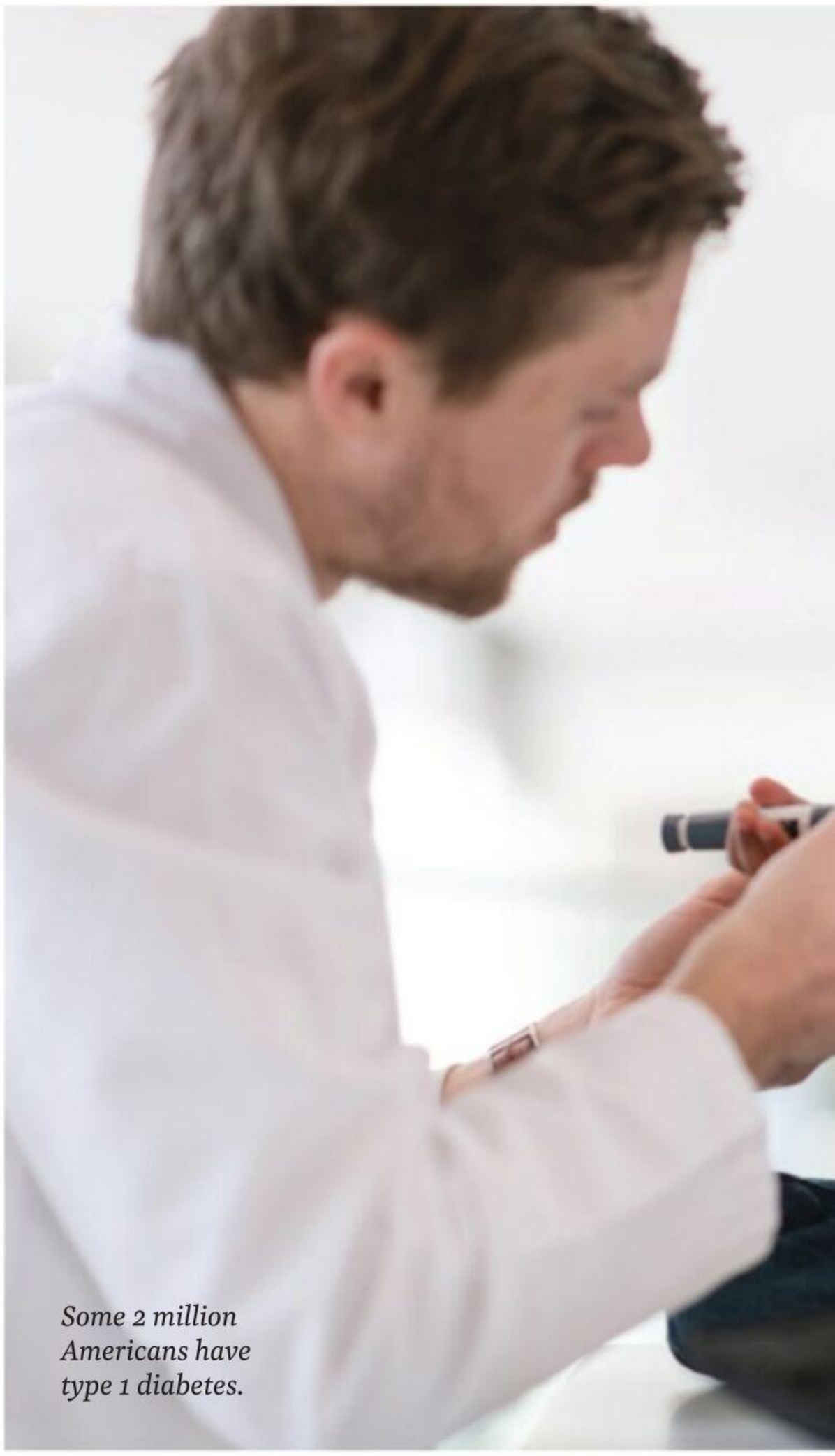
Until now, efforts to change the microbiome to address specific medical conditions have mostly involved fecal transplants. Studies have supported the idea that transplanting fecal matter from people with healthy gut bacteria can seed those good bacteria in the guts of people with less healthy makeups. But fecal transplants are tricky to develop and administer. Fecal matter is collected from healthy donors and treated in a series of purifying and sterilizing steps to ensure that only the desired populations of bacteria are transferred from one person to another, and it's then given rectally. However, some recipients develop infections from insufficiently purified fecal matter, and questions about the balance of benefits and risks continue to plague the approach.

Seres' product, which eliminates rectal administration, is also made from donated fecal material that is sterilized and processed—but it is in spore form, to contain a combination of bacteria that only activate once they reach the gut. The recipe, which took the company nearly a decade to perfect, features bacteria from the Firmicute phylum, one of the dominant populations of human gut bacteria.

DIABETES TYPE 1: A LIFELONG JOURNEY

UNLIKE TYPE 2, WHERE LIFESTYLE FACTORS MAY IMPAIR INSULIN PRODUCTION, TYPE 1 IS CAUSED BY THE IMMUNE SYSTEM ATTACKING CELLS THAT PRODUCE INSULIN.

BY ASHLEY ABRAMSON



Some 2 million Americans have type 1 diabetes.

ROB INTREGLIA WAS 11 YEARS OLD, thirsty all the time, and drinking so much water he was peeing every thirty minutes—even in the middle of the night. One day during gym class, the sixth grader felt so nauseous he was sent home by the school nurse and taken to the doctor by his mom. Within hours, Intreglia had been admitted to the hospital and diagnosed with low blood sugar and type 1 diabetes. "I didn't quite grasp the full concept," says Intreglia, now 33 years old and living in New York. "But I knew my life was never going to be the same."

For the 2 million Americans who have type 1 diabetes, the initial diagnosis can feel—and is—harrowing. The autoimmune disease, where the body attacks cells that produce insulin, causes dangerously high blood sugar and disrupts people's routines. It requires constant monitoring of carbohydrates and glucose levels, and daily boosts of insulin. Down the road, there's the prospect of medical complications ranging from nerve damage to kidney failure to blindness. "You can't take a day off from type 1 diabetes," says Srividya Kidambi, MD, an endocrinologist with the Froedtert and Medical College of Wisconsin health network. "People can develop fatigue because they're constantly managing blood sugar and can't miss their medication, which is a significant burden for them and their family members."

As common as the disease is, there are many misconceptions around it. Some people confuse type 1 with type 2—where lifestyle factors may impair insulin production—and then blame the type 1 patient for causing his own disease. Others may also assume, wrongly, the patient cannot eat sugar. Even medical professionals can err: In some cases, adults with classic risk factors for type 2 diabetes may actually have type 1 and be misdiagnosed.

The good news: The technology to treat type 1 diabetes is advancing, making treatment more streamlined and effective. Today, a person with type 1 who follows doctors' orders can expect to live a normal lifespan without severe medical complications. What follows is an explanation of what causes type 1 diabetes, how it can affect peoples' lives, and how the latest scientific advancements are transforming treatments.

LIVING WITH TYPE 1 DIABETES

Type 1 diabetes has been described in historical texts for thousands of years, with the most important advancements occurring since the late 19th century. In 1889, scientists conducted a famous operation in which they removed a dog's pancreas, causing severe and fatal diabetes, thus establishing the organ's role in developing type 1. A few years later, researchers extracted insulin from pancreatic cells and used it to treat type 1 diabetes patients. The new procedure saved millions of lives and became standard protocol, typically with patients responsible for monitoring their own blood sugar and administering insulin injections. As recently as the early 2000s, Rob Intreglia was measuring his blood sugar with a finger prick multiple times a day and giving himself insulin manually. "It was very regimented," he says. "I remember feeling frustrated on how strict my diet had gotten, in such a short amount of time."

Today, science has advanced to the point where the majority of type 1 diabetes patients keep tabs on their blood sugar levels without pinpricks or self-administered insulin injections. Instead, they wear a continuous glucose monitor that adheres to the skin and communicates via technology to an insulin pump that automatically dispenses the medication as needed,. "It's a rather dramatic change," says Graham T. McMahon, MD, an adjunct professor of endocrinology at Northwestern Feinberg School of Medicine. "The treatment isn't a panacea, but it's changed the standard of treatment for type 1 diabetes patients."

While it is generally accepted that type 1 diabetes is an immune disease, explanations for what causes it don't align perfectly. For example, people with a sibling or parent who have type 1 diabetes are more likely to develop it, suggesting a genetic risk factor. But some people with the genetic risk never develop it. The difference in outcomes means unique factors in a person's environment—such as a viral illness—can affect whether they ever get the disease, says McMahon.

There are two scenarios for diagnosis. In the majority of cases, people discover they have the disease when they develop symptoms of high blood sugar, such as extreme thirst and frequent urination. "Glucose is excreted in urine and pulls water with it, and then patients feel thirsty because they are peeing so much," explains McMahon. Sometimes people feel tired or weak—or lose weight unintentionally—because blood sugar isn't fueling organs. Less commonly, the disease manifests without any clear signs and only is discovered during routine blood work.

The same exceptions apply to timing. As in Intreglia's situation, type 1 diabetes most commonly shows up in childhood or adolescence. However, increasingly the condition is being diagnosed in adulthood,

as Lanise Shortell, a 52-year-old hospice nurse from Atlanta, discovered when she was 19 and pregnant. "I was so tired I felt like I was walking through mud with cement bricks on my feet," she says. A routine glucose tolerance test showed her blood sugar was high, and she started taking insulin. Doctors thought the disease would go away after Shortell's pregnancy, but she's been diabetic since.

Regardless of symptoms and timing, treatment is the same: Patients with type 1 diabetes need to monitor their blood sugar and take insulin every day, for the rest of their lives. Insulin pumps, which dispense a baseline amount of insulin each day, plus additional doses after eating, have improved life for people with type 1, but the technology is not perfect and patients still can experience dangerous rises or dips in blood sugar.

ONE PROMISING PROTOCOL CENTERS ON TRYING TO PROTECT PATIENTS FROM IMMUNE RESPONSES THAT OCCUR WITH ISLET CELL TRANSPLANTS.

The long-term effects of high blood sugar are concerning. Too much sugar in the body can damage organs and result in kidney failure, blindness, nerve damage, and an increased risk of heart disease. Too little glucose can trigger shakiness, dizziness, confusion, seizures, and fainting. Shortell, who wears a continuous glucose monitor and insulin pump, recently passed out while driving when her blood sugar plummeted. No one was hurt when her car slowly came to a stop on the street, but emergency medical services had to break open her car window and administer glucose. "The paramedics saved my life," she says.

In extreme cases, patients may experience a reaction called diabetic ketoacidosis (DKA), in which fat is broken down too rapidly for the body to process it and toxic levels of a fuel called ketones builds up in the person's blood. DKA, characterized by symptoms including labored breathing, headaches, vomiting, and stomach pain, can be life-threatening.

While most people with type 1 respond well to insulin and lifestyle factors, some need more help to manage the disease and work with a diabetes educator or specially trained nurses and dieticians. Shortell recently adopted a dog trained to detect changes in blood sugar, likely through scent and behavior, and says she hasn't had a medical emergency since.

If a patient does not respond to insulin injections, a pancreas transplant—sometimes paired with a kidney transplant—is an option, though there is no guarantee the procedures will work. "We're still trying to understand how to tamp down the immune response," says Philip Orlander, MD, a professor and endocrinologist with UTHealth Houston. "Even if you give a partial pancreas transplant from a twin that doesn't have diabetes to one who does, that pancreas would then develop type 1 diabetes because the immune response is still there."

Lastly, some choose an islet-cell transplant, which involves inserting insulin-making cells into a person's pancreas. But as with the transplant surgery, the procedure has challenges. In some cases, the immune system continues attacking the insulin cells, Orlander says, and any positive results are usually temporary, lasting a year or two.

THE FUTURE OF TYPE 1 DIABETES TREATMENT

Treatments for type 1 are always advancing, with the technology supporting glucose monitors and insulin pumps growing more efficient, and researchers finding new treatments to reduce the burden on patients' lives. One promising protocol centers on trying to protect patients from immune responses that occur with islet-cell transplants, in order to extend the period of time the procedure is effective. Several pharmaceutical companies are developing medications that put islet cells in "pouches" that evade immune detection, which can help restore normal insulin function.

Preventative measures are also evolving. For example, in November 2022 the FDA approved a monoclonal antibody, teplizumab, now marketed as Tzield, to help limit the immune activity in people with type 1 diabetes antibodies. Semaglutide, a drug often used for type 2 diabetes, has also been shown in studies to help delay insulin use in people with early type 1. Similar drugs are likely to come to market in future years. "Not having to take insulin day in and day out for a couple of years can be quite life changing for people," says Kidambi. ◻

PLAY THERAPY

A NEW BARBIE WITH TYPE 1 DIABETES IS THE LATEST MOVE BY THE TOY INDUSTRY TO APPEAL TO FAMILIES OF CHILDREN WITH THE CONDITION.

BY EILEEN DASPIN

She is a Barbie like the hundreds of other Barbies: fashionable, in a blue polka-dot dress with matching booties; well-coiffed, with shiny, cascading tresses; and prepared for her day, with a handbag to store her snacks, cell phone, and other things she needs.

What's different about this late-model Barbie, introduced in July 2025, is her health. Like 1.8 million young people around the world, the doll has type 1 diabetes. She wears a continuous glucose monitor (CGM) on her arm—held in place with heart-shaped tape—which is linked to her phone, mimicking real-life monitors that track glucose levels 24 hours a day via a sensor under the skin. "Barbie helps shape children's early perceptions of the world," said Mattel in a press release. "…By reflecting medical conditions like T1D, we ensure more kids can see themselves in the stories they imagine and the dolls they love."

With an increasing number of adolescents being diagnosed with type 1 diabetes, toy companies are seeking ways to both help the affected young people understand the condition and align themselves with a good cause. One of the first toys was Jerry the Bear, an interactive stuffed animal introduced in 2013 that teaches children about counting carbohydrates, monitoring blood sugar, and administering insulin. Build-a-Bear offers a three-piece diabetes kit with a plush insulin pump, lancing device, and glucometer. The LEGO Friends Sports Center includes a mini figure named Hanna who wears a CGM, while Marvin the Diabetic Monkey is a fidget toy that wears an insulin pump on his stomach. There are also bingo games, workbooks, and the lime green insulin beta cell, a cuddly stuffie that comes with an endocrine-system information card.

T1D toys are a tiny sliver of the $28 billion toy industry and often are offered by independent makers with a personal connection to diabetes. They are of a piece with merchandise aimed at helping young people with T1D feel less self-conscious and more empowered about their diabetes, whether that is CGM patches that come in colorful designs, futuristic watches, or eye-catching fanny packs that hold insulin pumps close to the body.

While the toys and other merchandise cannot cure or treat diabetes, they can help both people with and without diabetes, as studies have shown that playing with dolls and toys with a range of physical challenges can reduce systemic inequality for disabled people. For example, if a child plays with a doll that has diabetes, it can help them understand the challenges of people with diabetes that they meet in real life.

Mattel partnered with Breakthrough T1D, a diabetes-education organization, to design the new Barbie.

A HISTORY OF DIABETES THERAPIES

FROM THE FIRST SIMPLE GLUCOSE TEST TO TODAY'S HYBRIDS THAT COMBINE GLUCOSE MONITORS AND INSULIN PUMPS.

BY AVA ERICKSON

The first dose of insulin given to a person was administered in 1922.

1908
The first glucose test is developed to detect the presence of sugar in the blood. The process involves heating a urine sample and mixing it with a copper reagent; if sugar is detected, the urine changes color. This type of test will be used for almost 50 years.

1922
A 14-year-old who is dying from diabetes becomes the first person to be injected with insulin, in a Toronto hospital. Within 24 hours, the boy's blood glucose normalizes. Eli Lilly soon begins mass producing the drug and it is adopted quickly by the medical community.

1936
A slower-acting insulin, which helps stabilize blood sugar for longer periods of time, is introduced.

1945
A modified copper reagent tablet for urine glucose testing debuts. It measures the amount of sugar in the heated urine with a color chart.

1954
Boiling syringes and needles for re-use is cumbersome, and in 1954, Becton, Dickinson and Company launches the first disposable syringe. By the mid-1960s, a large number of disposable syringes are on the market, helping to curb the frequency of infection.

1956
Clinistix, the first dip and read strip, is launched. The product, which specifically measures glucose as opposed to simply detecting sugar in urine, and which has the reagents embedded in a paper strip, is a big step forward for people with diabetes.

1963
The prototype for the first insulin pump is developed by Dr. Arnold Kadish. The device is huge and carried like a backpack.

1965
The first blood glucose test strip is developed by Ames. It requires a large drop of blood and is not for home use.

1974
The first insulin pump, the Biostator, hits the market. The computer-based insulin infusion system is a welcomed advance, but its large size makes it difficult for outpatient use.

1976
The first wearable insulin pump debuts. Called the AutoSyringe, the device paves the way for insulin pump therapy, which aids in more precise insulin dosing and fewer injections. Over the next few years, many more wearable insulin pumps come onto the market.

1981
The first blood glucose meter, which integrates blood-glucose

test-strip technology and a digital display, is introduced. The device allows patients to test their own glucose levels at home. Self-monitoring blood glucose becomes a standard practice for diabetes care.

1982
The first biosynthetic human insulin is created, resolving the supply and price issues of utilizing animal insulins.

1985
The first insulin pen, a more accurate, convenient, and discrete injection system than a syringe, is brought to the market.

1992
The year marks the arrival of the MiniMed 506, a more advanced "smart pump," with technology such as meal-bolus memory (indicating the dose of insulin needed before a meal) and a daily insulin tabulator. Throughout the 1990s, pumps grow smaller and more efficient.

1999
A continuous glucose monitor (CGM) is approved for the first time by the FDA. The device takes constant readings and sends the data to a health care provider for review.

CGM systems alert patients to insulin levels in real time.

2004
Medtronic introduces the Guardian REAL-Time CGM system, which notifies the wearer immediately of high or low blood glucose.

2006
The launch of Medtronic's MiniMed Paradigm REAL-Time System, an integrated pump with both a CGM and an insulin pump. Patients are alerted of glucose information in real time so they can adjust insulin delivery accordingly.

2007
Second-generation pens hit the market. These smart pens have a memory function that allows them to store date, time, and dosage information.

2016
The FDA approves the MiniMed 670G, the first hybrid closed loop system. Made up of a CGM and insulin pump, the device automatically adjusts insulin delivery based on glucose data.

2019
The first interoperable insulin pump is introduced by Tandem Diabetes Care. Called an alternate controller enabled pump, it is able to link various different types of diabetes therapy systems to manage treatment.

2023
Tandem's 2023 pump is less than half the size of the previous model. It is small enough to fit in a coin pocket and receives a special mention in TIME's Best Inventions of the year.

Disposable syringes were introduced in 1954.

CHAPTER 2

THE DIABETES-BODY CONNECTION

HIGH GLUCOSE LEVELS ARE ASSOCIATED WITH A RANGE OF HEALTH CONDITIONS. WHAT YOU NEED TO KNOW.

THE LINK BETWEEN HEART DISEASE AND DIABETES

HIGH BLOOD SUGAR LEVELS CAN HARM YOUR HEART AND BLOOD VESSELS.

BY MARKHAM HEID AND LALA TANMOY DAS

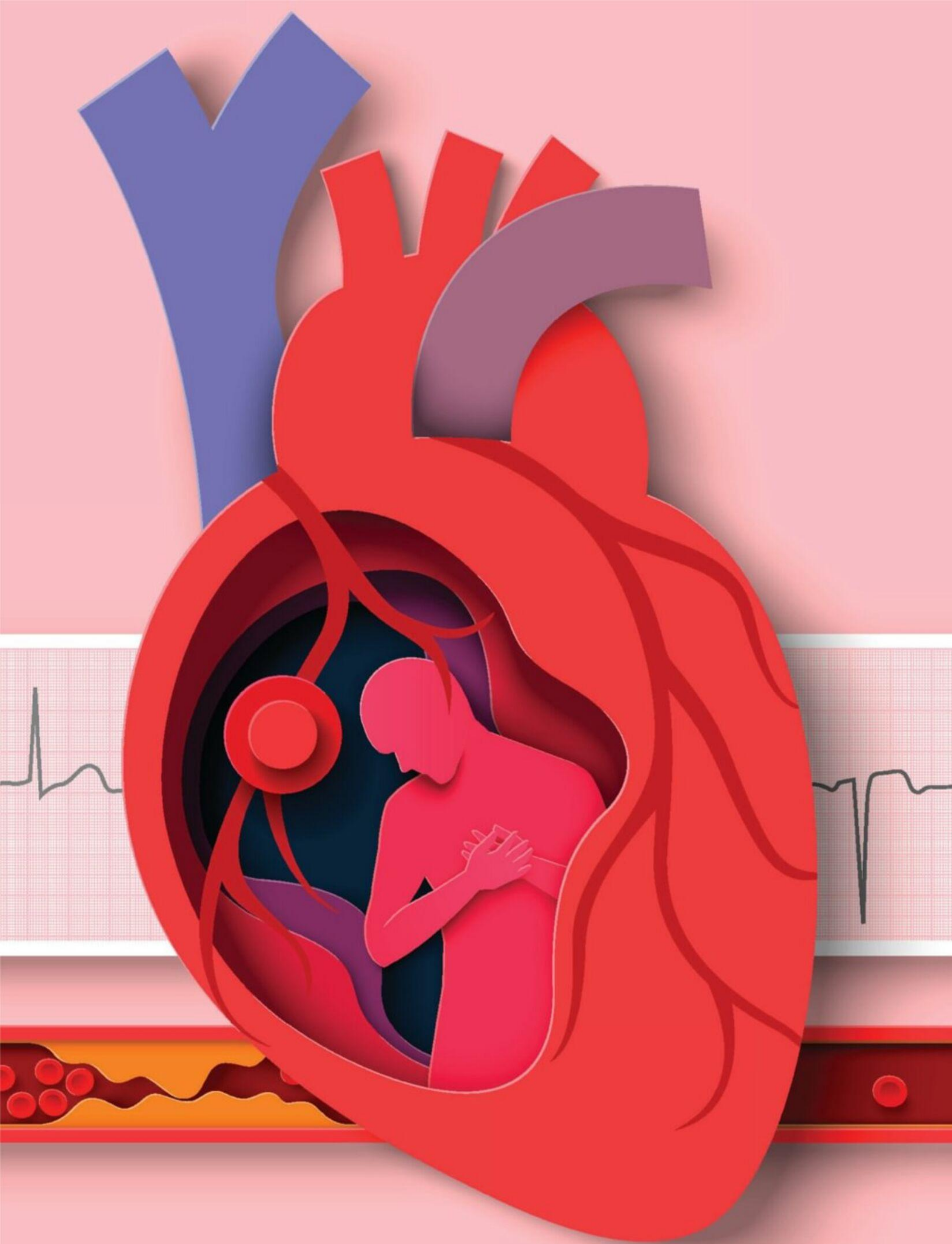
LEFT UNTREATED—EVEN FOR A SHORT period of time—the high blood sugar levels that accompany diabetes can impair blood vessels and lead to complications including heart failure, heart arrhythmias, and peripheral artery disease. Here is what you need to know.

DIABETES AND HEART FAILURE

Diabetes—caused by high blood glucose and insulin levels that can damage the heart and blood vessels—puts a person who has the disease at a high risk for issues that occur when the heart muscle is unable to pump sufficient blood and oxygen to the body. Known as heart failure, the condition can cause the buildup of fluid in the lungs, abdomen, and limbs, and cause organs to shut down. The health risk to a person with diabetes is compounded by the fact that the disease also has been linked to mitochondrial dysfunction, oxidative stress, inflammation, and an increase in the formation of harmful compounds called advanced glycation end products (AGE), all of which can contribute to the development of heart failure.

In fact, up to 22 percent of people with diabetes will develop heart failure, according to a June 2022 report from the American Diabetes Association, and the incidence of heart failure within the diabetes community, including people with type 1 or type 2, is increasing. A study published in the *European Journal of Heart Failure* of more than 36,000 people found that median survival was reduced by more than a year among those who had both heart failure and type 2 diabetes compared to those with heart failure alone. Heart failure, concluded the report, is "an underappreciated complication of diabetes."

Whether a person has diabetes or not, the symptoms of heart failure tend to be the same. They include shortness of breath, when you're active or at rest, wheezing, weight gain, and persistent cough. Fatigue lands at or near the top of the list, and may be subtle at first. "Someone may just feel like they don't have the same energy they used to," says Dr. James Januzzi, a professor of medicine at Harvard Medical



School and a clinical cardiologist at Massachusetts General Hospital.

The problem is that shortness of breath may be difficult to spot if a person's fatigue has caused them to cut down on physical activity. "Frequently I'll ask a patient if they get shortness of breath, and they'll say no, but it's because they've reduced their activity," says Januzzi. As heart failure progresses, the symptoms tend to become much more noticeable.

As the disease progresses, the person may even experience shortness of breath when lying down or may be awakened from sleep by difficult breathing. "This has to do with fluid overload in the lungs as a result of the heart not pumping the way it should," says Dr. Amgad Makaryus, a professor of cardiology at the Zucker School of Medicine at Hofstra/Northwell, in New York. Fluid overload associated with heart failure, he adds, can also lead to swelling (edema) in the legs or abdomen.

Other signals include weakness, a rapid or irregular heartbeat, nausea, and problems thinking or concentrating—symptoms that tend to become more pronounced with time. "The fatigue may become so great that someone can't complete their daily activities," Makaryus says.

While many cases of heart failure pass through an early stage without noticeable symptoms, certain blood tests may be able to detect them at this stage. "Early diagnosis can help make sure that people with diabetes have access to the best treatments at the right time," whether that's new drug therapies or switching out medications that may be contributing to the problem, says Dr. Rodica Pop-Busui, a professor of diabetes at the University of Michigan and a board member of the American Diabetes Association.

Medication, prescribed based on the severity of the condition, is the standard, first-line approach. "We look at something called the ejection fraction, or the squeezing strength of the heart, to determine the appropriate treatment plan," Januzzi says. If a patient's ejection fraction is reduced—meaning their heart is not pumping as strongly as it should—treatment usually includes several classes of drug that are designed to widen blood vessels and improve blood flow. These include beta blockers, aldosterone blockers, a medication called sacubitril/valsartan, which widens blood vessels, and what's known as an SGLT-2 inhibitor, which not only lowers blood pressure but also helps reduce blood glucose levels. (SGLT-2 inhibitors are often used to treat diabetes even absent heart failure.)

"For people with preserved ejection fraction, meaning abnormal squeezing strength, therapeutic options are more limited," Januzzi says. "Recent clinical trials of SGLT-2 inhibitors showed benefit in these individuals, so these should be now considered in anyone with heart failure, but especially in people with diabetes." He adds that GLP-1 drugs—such as Ozempic and Rybelsus, which have been in the news lately—have also demonstrated benefit in people with both diabetes and heart failure, and are likely to be used more frequently to treat these co-occurring conditions.

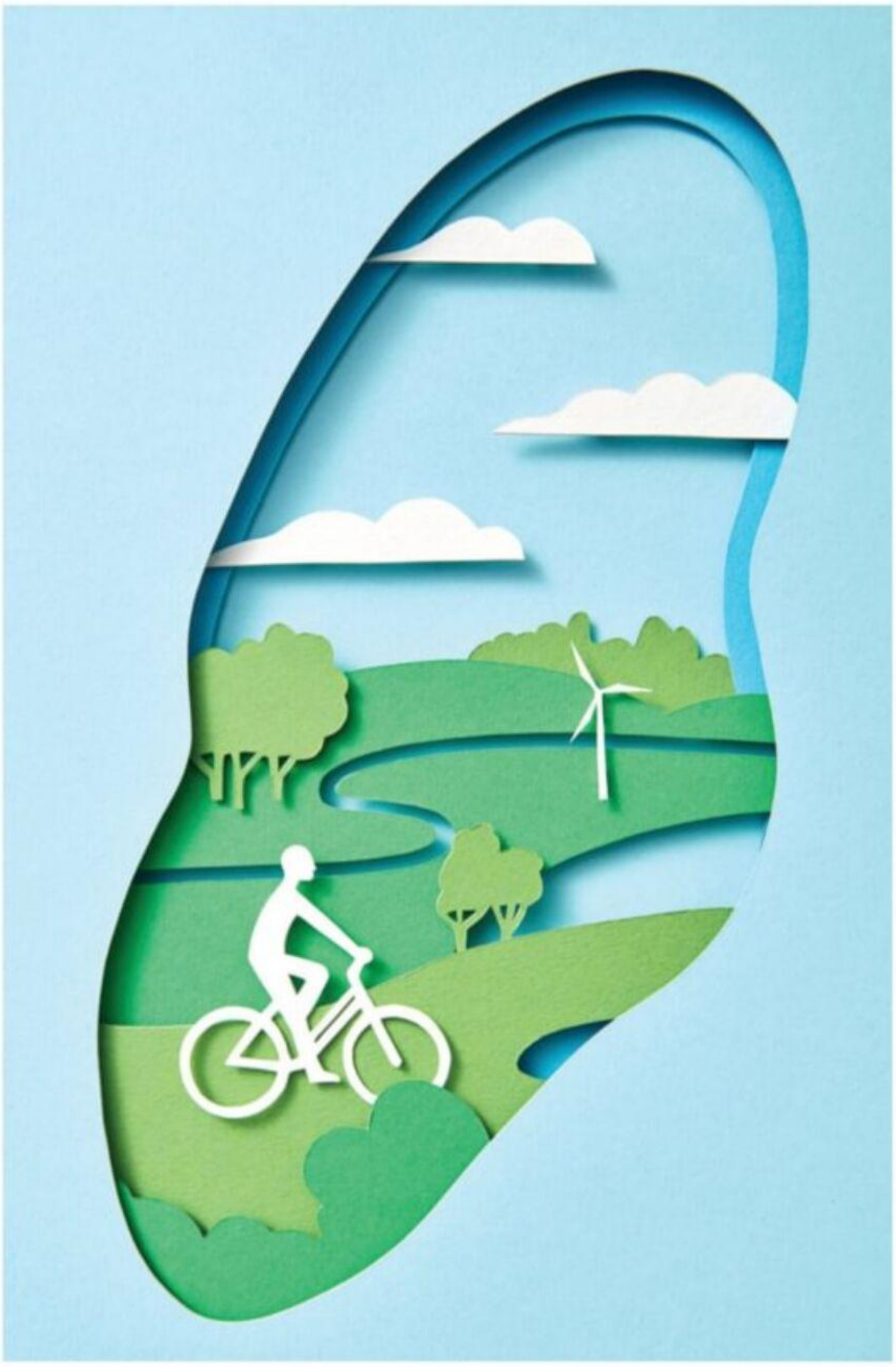
Apart from drugs, lifestyle and behavioral changes can make a meaningful difference for people with heart failure. "This includes increasing exercise whenever possible," Januzzi says. "This also includes paying attention to one's mood." Depression and anxiety are both associated with poorer outcomes in people with heart failure, he says, so it's necessary to address these mental health challenges (with therapy, for example) if they appear. A Mediterranean-style diet that includes more complex carbohydrates and a judicious amount of protein is often recommended, as is working with a medical dietitian or nutritionist to create a customized eating plan.

DIABETES AND HEART ARRHYTHMIAS

The human heart beats roughly 3 billion times during the course of an average lifetime. Every single time it beats, blood is drawn into its two upper chambers, held there briefly by a network of valves, and then pumped out forcefully through its two lower chambers. This drawing-and-pumping action ensures that about six liters of freshly oxygenated blood leaves the heart and enters the bloodstream every minute—a volume that can rise to more than 35 liters per minute when someone is exercising.

But none of that can happen unless the heart's complicated machinery—its assorted valves and muscles and electrical circuitry—is working in harmony. When that harmony breaks down, the heart can pump too fast or too slow, or it can lose coordination among its various chambers. This breakdown is known as an arrhythmia, which can lead to complications ranging from fatigue or shortness of breath to heart attack or stroke.

"When we say arrhythmia, we literally mean the heart is out of rhythm," says Dr. Jonathan Piccini, a



cardiologist and arrhythmia specialist at Duke University Medical Center. He compares the heart's operation to a symphony orchestra. "If someone was playing off the wrong sheet of music or if their instrument were out of tune, that would not be subtle. It would be profoundly disruptive," he says. "The same is true of a heart arrhythmia."

Heart arrhythmias are common; up to 5 percent of the general population have some form of the condition.

The most common form, by far, is atrial fibrillation, or Afib. This type of arrhythmia arises in the upper chambers of the heart. "Between 60 and 100 beats per minute is normal," Piccini says. "In Afib, the top regions of the heart are in total chaos and could be beating on the order of 400 to 600 beats per minute."

The Framingham Heart Study is one of the most famous and fruitful research efforts ever undertaken. It began in 1948 with 5,000-plus study participants—all from the town of Framingham, Massachusetts—and continues to this day. The purpose of the study is to track participants' health and lifestyles over time in order to uncover potential risk factors for heart disease. Thanks in large part to the Framingham Heart Study, researchers recognized that smoking, high blood pressure, too little physical activity, and many other variables could raise a person's risk for heart disease.

Almost 30 years ago, data from the Framingham Heart Study helped reveal that people with diabetes are at increased risk for Afib. However, the connection between the two conditions has only recently garnered serious research attention. "This is an area of tremendous interest, primarily because we have discovered newer classes of medications that, in addition to lowering glucose, can also reduce the risk of heart complications," says Dr. Jennifer Green, a diabetes and metabolism specialist at Duke University who, along with Piccini, has conducted research on diabetes and Afib. More work is needed to determine exactly why people with diabetes are at increased risk for Afib, "but there does seem to be a cause-and-effect relationship between the two," says Green.

One hypothesis is that elevated levels of blood sugar (glucose), which is a hallmark of diabetes, causes damage to the heart that may result in arrhythmias. "There are things we call advanced glycation end products"—harmful compounds that arise when blood sugar combines with blood proteins or fats—"that we know can be responsible for organ damage," Green explains.

Another hypothesis is that diabetes contributes to the development of high blood pressure (hypertension), which may cause damage to the heart in ways that result in an arrhythmia. "Diabetes affects the blood vessels in ways that make them stiffer and that makes blood pressure rise," says Dr. Mattias

Brunström, a hypertension specialist and physician researcher at Umeå University, in Sweden. Roughly two thirds of adults with diabetes also have hypertension, and people with hypertension are almost twice as likely to develop Afib as people who do not have hypertension.

Yet another possibility is that diabetes-related inflammation may contribute to the development of an arrhythmia. "In people with diabetes, there are both systemic and localized increases in inflammation that, if severe enough and prolonged enough, could increase the risk of arrhythmia," Green says. All of these theories could be accurate. "It's probably not just one mechanism or one explanation, but several," she says.

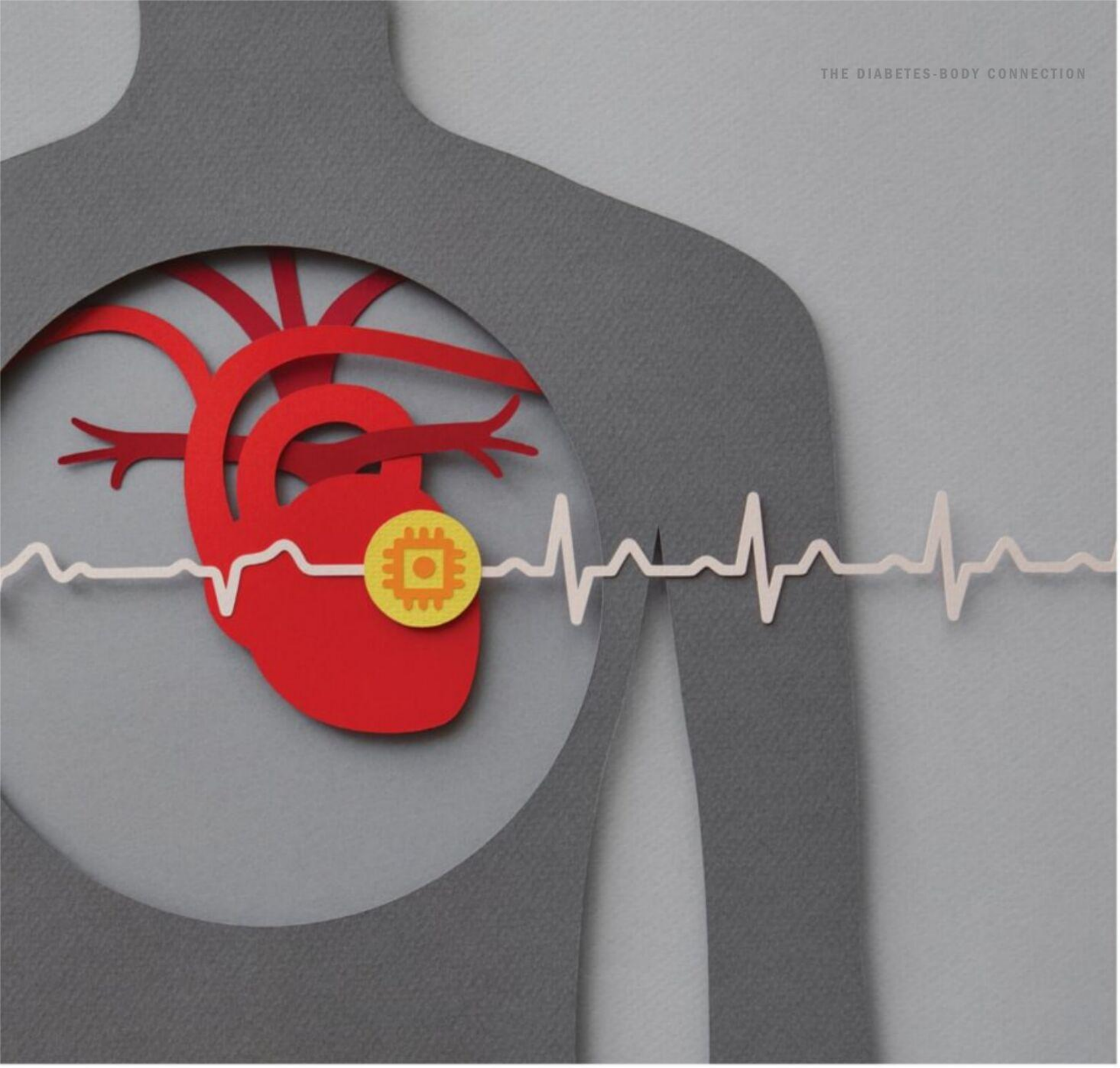
There is good evidence that people who have well-controlled diabetes are much less likely to develop Afib or other types of arrhythmias than people who have poorly controlled diabetes. One key strategy—keeping blood sugar at a healthy level—could be the best way for a person with diabetes to manage the disease and prevent an arrhythmia. "There's some evidence that certain classes of diabetes drugs, such as SGLT-2 inhibitors, may reduce the risk of atrial arrhythmias," Green says.

There are also some drugs that are aimed specifically at reducing the risks of heart complications in people with diabetes. For example, some work has found that a drug called finerenone may lower the likelihood that someone with diabetes will go on to develop heart complications, including an arrhythmia. "This drug helps counteract inflammation, and may provide a benefit through that process," says Green.

More follow-up is needed. "A lot of what's been published already are analyses of observational data, meaning looking at outcomes among people receiving the drugs and seeing how they do," says Green. "That information can be helpful, but we need randomized controlled trials to see if these drugs really do reduce risks."

Piccini echoes her assessment. "There really haven't been any studies expressly asking, does treatment with one of these lead to better outcomes?" he says. These sorts of studies are in the works, he adds, but we don't have answers yet. In the meantime, Piccini notes that people with diabetes who are concerned about heart complications, including arrhythmias, should focus on controlling their blood sugar as well as their overall health. That means taking their diabetes medications as their doctor advises, and also trying to eat right, exercise, stop smoking, and maintain a healthy body weight. "Don't drink to excess, and get plenty of sleep," Piccini adds.

Given how the landscape of treatments has evolved in the last decade, people with type 2 diabetes should ask their care providers about medications that have been shown to reduce heart-related complications; and doctors should consult guidelines updated annually by the American Diabetes Association. "I think it is time for everyone, clinicians in particular, to reassess whether the regimens they are prescribing are the most effective for their patients," says Green. "A person with diabetes should ask their doctor whether they are on the guideline-



recommended therapy, because unfortunately, many are not," she adds.

For a person who has been diagnosed with both diabetes and a heart arrhythmia, the situation is much the same. Some drugs have shown promise in treating both conditions, but experts say more work is needed. As Piccini puts it, "If someone has Afib and diabetes, should we be using some medications in preference to others? This is an area where we need more information."

Setting aside treatments that target both conditions, there are a number of effective ways for doctors to handle an arrhythmia—regardless of whether a person has diabetes. One technique called electrical cardioversion uses low-energy electrical pulses—shocks, basically—to help reset and normalize the heart's rhythm. The introduction of a pacemaker or other less-invasive procedure can also resolve or reduce the risks of an arrhythmia.

DIABETES AND PERIPHERAL ARTERY DISEASE

The arteries that branch out and feed into our arms and legs make up the bulk of what we call peripheral arteries. When there is buildup of fatty plaques in the arteries, the vessels narrow and the legs or arms receive insufficient blood flow. The result is a condition called peripheral artery disease (PAD), which affects nearly 12 million people in the U.S.—a third of whom also have type 1 or type 2 diabetes. While data is insufficient to show if either type is more concretely linked to PAD, "type 2 diabetes is

more common, simply because there are more type 2 diabetic patients," says Dr. Samuel Kim, a preventative cardiologist and lipidologist at Weill Cornell Medicine in New York.

Diabetes is a key factor in PAD because of the persistent inflammation—detectable in high levels of C-reactive protein in the blood—that accompanies the disease. Some studies have shown that high levels of the C-reactive protein may enhance clotting within arteries, making them even more susceptible to narrowing and blockages. Additionally, high levels of sugar in blood—a characteristic of inadequately controlled diabetes—produces unstable molecules that ricochet within cells and damage DNA and RNA. Protein kinase C (PKC), one generator of these reactive oxygen molecules, also has been shown to harm the structure and function of blood vessels.

GIVEN HOW UNRELIABLE SYMPTOMS CAN BE, IT BECOMES ALL THE MORE IMPORTANT FOR PEOPLE WITH DIABETES TO GET AN ANNUAL DIABETIC FOOT EXAM, SAYS ONE VASCULAR SURGEON.

Kim emphasizes the negative impact of diabetes on endothelial cells, which line the inner layer of blood vessels. When healthy, the endothelial cells produce a gaseous molecule called nitric oxide, which helps blood vessels stretch and recoil as needed, and mellows chemical signals that cue our bodies to inappropriately clot blood. When exposed to high amounts of sugar, these cells lose their ability to modulate nitric oxide levels—and the complex architecture of blood vessels, along with their astonishing pliability, is severely compromised.

Because of factors including poor blood-sugar control, smoking, unhealthy diet, physical inactivity, and genetics, the linings of blood vessels can be frayed long before diabetes is officially diagnosed. Studies have consistently found that the duration of diabetes corresponds with the extent of arterial damage. Plus, each 1 percent rise in an A1C test—a test that measures the amount of sugars chemically bound to blood cells (compared with sugars floating in the bloodstream, as measured by a regular blood-glucose test)—is associated with an almost 30 percent increased risk of being diagnosed with PAD.

Race and ethnicity also play a role in developing this duo of diseases. "If you have diabetes and you're Black, your risk of PAD is almost twice as high as Caucasians," says Dr. J. Antonio Gutierrez, an interventional cardiologist at Duke Health who is also involved in patient-outreach activities among minority communities outside of Durham, North Carolina. Hispanic, Puerto Rican, and Mexican people are also at increased risk, he says.

"Only a third of patients have the classic textbook symptoms," says Gutierrez, "for others, the symptoms may be a lot more subtle." Most common, people experience throbbing, cramping, or a burning sensation in their legs—particularly in their calves—with walking or exercise, and find that it improves within a few minutes of resting."You could have buttock pain, which would mean it's a proximal vessel you could be dealing with, or pain in your thighs or somewhere further down your feet," Kim says.

Patients may experience some degree of hair loss on their lower legs, changes in skin and toenails, and/or temperature differences between their feet, according to Dr. Aaron Aday, a cardiologist and vascular-medicine specialist at Vanderbilt University Medical Center, in Nashville. In cases of poor diabetes management, PAD can progress to patients having blisters, nonhealing foot ulcers, infections, and tissue death, ultimately requiring amputations. Even people who are conscientious about their diabetes management can live with undetected PAD because they have problems with their nerves.

Consider Tennessee high school basketball and softball coach Steve Shipley, first diagnosed with type 1 diabetes in 1977. About eight years ago, when Shipley was in his early 60s, he noticed several blisters under his toes after umpiring softball. Having never had any similar symptoms or experienced unusual leg pain or cramping, he remained active, coaching basketball and softball, while playing and refereeing those sports recreationally. "I noticed the blisters and thought, 'Well, it's probably from the shoes rubbing against that area,'" Shipley says.

After a couple of days, when the blisters looked worse, the coach made an appointment with his podiatrist, and together they agreed Shipley should try

platform shoes with Velcro straps, designed to prevent any rubbing of the toes. Still, the blisters didn't heal, and one evening Shipley noticed his toe turning dark. He returned to the podiatrist, who had to perform an emergency surgery. "I'm glad I went when I did, because if I'd waited any longer, I might've lost my entire leg instead of just one toe," he says.

Given how unreliable symptoms can be, it becomes all the more important for people with diabetes to get an annual diabetic foot exam, says Dr. Philip Goodney, a vascular surgeon at Dartmouth Hitchcock Medical Center, in Lebanon, New Hampshire. During these visits, medical providers ask detailed questions about diabetes management, lifestyle factors like smoking and diet, and movement difficulties. A doctor might order a noninvasive test, the ankle-brachial index, which can help determine the severity of arterial disease. This test is usually done in a resting position, but patients are sometimes asked to run on a treadmill to better locate symptoms. The provider might also conduct an anatomic evaluation—through ultrasound, CT scan, or magnetic resonance angiography—to visualize the location and extent of blockages more precisely. Along with the patient's history and physical exam, these scans may better inform the nuances of a treatment plan.

There are several treatment options for peripheral artery disease. Many people with PAD are instructed to start supervised exercise therapy. "You push people to exercise beyond the boundaries of what they can tolerate," Kim says. "The idea here is that over time, your body builds collateral blood vessels that take detours around the clogged vessel." Such a program can be done at home—by going on walks for short to moderate distances—or in a rehabilitation center. "At the same time, it's also important to ensure that people's diabetes is properly managed, their blood pressure is under control, they've stopped smoking, and they're eating healthfully to lower cholesterol," Aday says.

American Heart Association/American College of Cardiology guidelines recommend that patients with PAD make exercise and lifestyle modifications and start on medications. Depending on the extent of blockages, however, medications alone may be insufficient, and surgical interventions may be necessary. "We can help reopen arteries with things like balloons, stents, or catheters, where patients can have quite dramatic effects," Goodney says. "But for those with more advanced disease who have failed balloons and stents, we can help rebuild the arteries, similar to a bypass surgery."

In some time-sensitive scenarios, amputation may be necessary. "When a patient is very ill, and all solutions to rebuild their arteries are used up without success, then removing a limb may be the only avenue left to get rid of severe pain or a life-threatening infection," Goodney says. Diabetes-related amputation can cause intense feelings of guilt, low body image and self-esteem, and depression. It's often a good idea for these patients to seek behavioral health services.

Shipley felt self-conscious for months following his toe-amputation surgery. "It makes you feel different," he recalls. "For example, if I was at the pool or if I didn't have my shoes on and somebody came to the door, I'd make sure I put them on before seeing them."

The emotional burden was even heavier around people at home. "Ironically, when I first had it, our granddaughter was only a couple of years old, and I was really afraid that the missing toe would scare her," he says. But by accident, she noticed it one day and said, "'Papaw, I would give you my toe if I could.' And from that moment, my mental outlook changed completely." □

THE MENTAL HEALTH CONNECTION

RESEARCH SUGGESTS THAT PEOPLE WITH PSYCHIATRIC DISORDERS HAVE HIGHER RATES OF TYPE 2 DIABETES, AND THE MEDICAL COMMUNITY IS INTEGRATING TREATMENTS.

BY SANDEEP RAVINDRAN

HAVING A MENTAL-HEALTH DISORDER is challenging enough without adding physical ailments to the mix. But recent research suggests that people with psychiatric disorders have higher rates of type 2 diabetes, and the combination can be devastating.

"When people who have preexisting mental illnesses develop diabetes, their outcomes are much worse," says Anne Doherty, an associate professor of psychiatry at University College Dublin. Compared to a person with type 2 diabetes who doesn't have a mental illness, "they are more likely to develop complications, and they're significantly more likely to die younger." The relationship goes both ways; people with diabetes also tend to have higher rates of psychiatric disorders and face worse outcomes than people without diabetes.

As doctors and researchers strive to untangle the mechanisms underlying these links, they're starting to integrate the treatment of these disparate diseases. "There are some studies that show that by treating depression aggressively and assertively, you can actually improve people's diabetes control—and, overall, their lives—so it's really quite exciting," Doherty says.

The association between diabetes and psychiatric disorders highlights the close connections between mental and physical health. An improved understanding of these connections could give us a better shot at preventing or treating such conditions.

Researchers have known for a while about the connection between certain severe psychiatric illnesses, such as depression or schizophrenia, and higher rates of type 2 diabetes, but a recent study by Nanna Lindekilde, a Ph.D. student at the University of Southern Denmark, went further. After analyzing 32 systematic reviews of the diabetes–mental health connection—based on 245 primary studies conducted between 1980 and 2020—Lindekilde and her colleagues found an increased risk across a broad range of psychiatric disorders.

For example, they found a 39.7 percent rate of type 2 diabetes among people with a sleep disorder and a 20.7 percent rate among those with a binge-eating disorder—significantly higher than the 6 percent to 9 percent incidence of type 2 thought to affect the global population. The researchers also found high rates of type 2 diabetes among people with substance-use disorder (15 percent), anxiety disorder (13 percent), bipolar disorder (11 percent), and psychosis (11 percent).

What's more, the association between type 2 diabetes and many psychiatric disorders goes both ways. For example, studies have shown that people with depression are more likely to get diabetes, and people with diabetes are more likely to get depression. The mechanisms underlying this two-way relationship are a mystery, but researchers are exploring intriguing hypotheses.

DECIPHERING COMPLEX UNDERLYING MECHANISMS

Psychiatric disorders and chronic illnesses like diabetes are known to take a psychological toll on patients, which can contribute to the risk of each. "People with psychiatric illnesses often smoke more, they may have poor nutrition, lower physical activities, so you get these knock-on effects on your physical health," says Seena Fazel, a professor of forensic psychiatry at the University of Oxford. For instance, depression can make it harder to exercise, eat healthy, or adhere to a medication regimen, all of which can increase diabetes risk.

Sleep is also known to be crucial to proper metabolic function. Psychiatric disorders can disrupt sleep and impair a person's metabolism, leading to an increased risk of diabetes. Plus, certain psychiatric medications can cause weight gain and difficulty managing blood sugar, leading to a higher risk of type 2 diabetes. "In some cases, the treatment for a mental illness can actually exacerbate underlying metabolic problems," Fazel says.

On the other hand, chronic illnesses such as diabetes can contribute to worse mental health. "Living with a chronic condition can lower your mood and also sometimes lead people to self-medicate with alcohol and drugs," Fazel says. "People with diabetes may be more likely to get depression because of the psychological effects of the illness, such as the restriction on certain things you can do and the sort of prognosis that you think may be hopeless."

Researchers have also recently gleaned tantalizing hints about common biological pathways that may underlie both diabetes and psychiatric disorders. Shared genetic pathways could be a potential culprit, but existing studies are too few and too small to make any definitive conclusions.

Researchers have been particularly interested in the potential genetic overlap between schizophrenia and type 2 diabetes as a way to explain higher rates of diabetes in people with schizophrenia. "While it is highly likely that there are overlapping genetic mechanisms, our understanding of this architecture remains limited," says Amir Sariaslan, a senior research fellow in psychiatric epidemiology at the University of Oxford. Inflammation is another likely suspect underlying both diabetes and psychiatric disorders.

"A STUDY OF MORE THAN 250,000 PEOPLE FOUND A SIMILAR INCREASE IN MORTALITY AMONG PATIENTS WITH PSYCHIATRIC DISORDERS WHO ALSO HAD CHRONIC CONDITIONS.

Chronic inflammatory responses are associated with a higher risk of developing type 2 diabetes, whereas certain markers of inflammation are found at higher levels in people with psychiatric disorders, such as depression. Scientists are investigating various inflammatory pathways and molecules to see if they might underlie both diabetes and psychiatric disorders. "It's definitely attracting a lot of research interest," Fazel says.

Scientists are also focusing on the role of the 100 trillion or so microbes in our guts and their associated genomes, collectively known as the gut microbiome. There are hints that changes to the gut microbiome can affect the brain and metabolism, theoretically influencing diabetes and psychiatric disorders.

But what we know about these links is still very preliminary, particularly in humans. "A lot of the research is happening at a lab level, and there's probably a ways to go before it's fully applied to human populations," Doherty says. "I think we're going to know an awful lot more about this area in five years' time."

It's challenging to run large trials of people with psychiatric illnesses, let alone when these patients also have diabetes, but large population studies could provide hints about some of the mechanisms underlying both disorders. Lindekilde is conducting a study of 250,000 Danish individuals to investigate potential mechanisms that might explain the association between a broad range of psychiatric disorders and type 2 diabetes.

Learning more about which mediating mechanisms play the biggest role and whether the mechanisms differ across psychiatric disorders is important and could help with future initiatives to prevent or manage these disorders, she says.

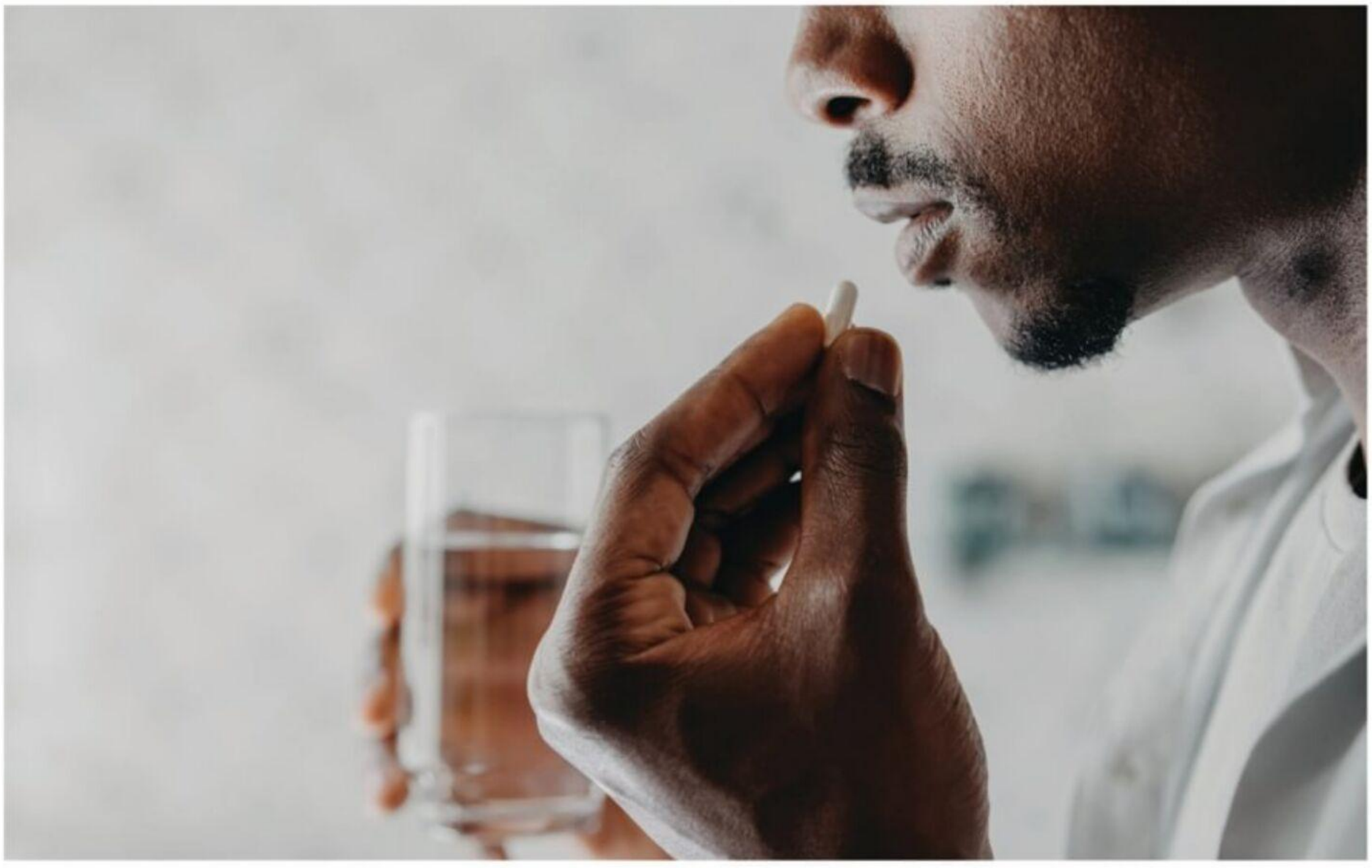
WORSE WHEN THEY'RE TOGETHER

Psychiatric disorders and diabetes are all independently associated with dying at a younger age. "On average, people with severe mental illness die 17 years younger than everybody else, which is a massive mortality gap," Doherty says. And people with diabetes generally live 7.5 years less than those without the disease, with even greater effects among those who get diabetes at a younger age. But having both can be particularly harmful.

"When people who have preexisting mental illnesses develop diabetes, their outcomes are much worse," Doherty says. She points to a study of patients at a London clinic that treats diabetes complications. When researchers evaluated all clinic patients for depression, they found that those with major depression were more than three times as likely to die after 18 months than those without major depression.

In a recent population study of more than 250,000 people in Sweden, Fazel found a similar increase in mortality among patients with psychiatric disorders who also had chronic conditions such as respiratory problems, cardiovascular disease, and diabetes. He found that the risk of dying within five years increased dramatically for people with diabetes when they also had a psychiatric disorder, such as depression.

To adjust for background factors such as ethnicity, family environment, and socioeconomic status, Fazel compared mortality among siblings with dia-



Studies have shown that people with depression are more likely to get diabetes, and vice versa.

betes, one with a psychiatric disorder and one without. "The interesting thing is elevated mortality risk still exists even if you account for these sibling models," Fazel says.

Fazel and others are still investigating why the combination of diabetes and psychiatric disorders leads to increased mortality. Some potential hypotheses are that psychiatric disorders may lead to delays in seeking diabetes treatment or difficulty adhering to diabetes treatments.

"I think these mechanisms are really very important, because that's where you can actually start to address and prevent the increased mortality," Fazel says. "The mortality risks are very high, and that's really a signal that this is an important challenge for health care systems to address."

AN INTEGRATED APPROACH

Researchers are increasingly considering integrated approaches to treating diabetes and psychiatric disorders, which hopefully will boost early detection and result in improved outcomes. "Both conditions have to be managed together if possible," Doherty says. Not only should mental-health care be a big part of diabetes care, she says, good physical monitoring should be embedded in mental-health clinics. Some countries, such as the United Kingdom, have started to include mental-health screening in diabetes care, but it's still far from common.

Such integrated approaches have shown some success in the U.S. and the U.K. Doherty took part in a U.K. program called Three Dimensions for Diabetes that wove together mental health, social care, and diabetes treatment and provided mental-health care for diabetes patients. "It was actually extraordinary, the proportion of people that we found to have significant mental-health problems that hadn't previously been diagnosed, and the one marker was the fact that they just weren't able to manage their diabetes," says Doherty."We found a significant improvement in diabetes control," she says.

Future studies will continue to study the link between type 2 diabetes and a wide range of psychiatric conditions, with the goal of finding common approaches to managing or treating both. The connection between these two seemingly unrelated disorders just goes to show how our mental and physical health are inexorably intertwined. "It argues against this division that you've either got mental or physical health problems, because actually they do overlap," Fazel says. □

THE HYPERTENSION CONNECTION

EXPERTS ARE STILL TRYING TO UNDERSTAND THE LINK BETWEEN TYPE 2 AND HIGH BLOOD PRESSURE AND BELIEVE EXCESS WEIGHT MAY PLAY A ROLE.

BY MARKHAM HEID

HIGH BLOOD PRESSURE—ALSO KNOWN as hypertension—and type 2 diabetes are two of the most common medical conditions in the United States. Unfortunately, they often occur together. Research has found that 85 percent of middle-aged or older adults who have type 2 diabetes also have hypertension, and both conditions elevate a person's risk for heart disease, stroke, and kidney disease.

These increased risks are significant and, in some cases, grave. Researchers have found that people with type 2 diabetes are up to four times more likely to develop cardiovascular disease than those who don't have the condition. People with diabetes are also twice as likely to die of cardiovascular problems. The leaps in rates of stroke, kidney failure, and other deadly complications are also substantial for people who have both high blood pressure and diabetes.

Why do these conditions so often show up in tandem? Experts are still trying to nail down the precise connections, but they say excess weight may play a part. Many people who have hypertension and type 2 diabetes also have obesity, and this "triumvirate," as some researchers have termed it, is associated with metabolic and endocrine problems that overlap and promote disease. "Obesity seems to be fertile soil for both," says Dr. Srinivasan Beddhu, a professor of internal medicine at the University of Utah School of Medicine.

Also, the prevalence of hypertension all but ensures that most people with type 2 diabetes will end up with both diseases. Roughly half of all U.S. adults have hypertension, and that percentage goes up with age. "It can develop as early as [ages] 30 to 42, but in most cases, by the time you're in your 50s, it's there," says Dr. George Bakris, a professor of medicine at the University of Chicago. Although hypertension often precedes type 2 diabetes, Bakris says, diabetes is increasingly common in young adults and even children. It's more important than ever to keep an eye out for both conditions, perhaps especially if you're overweight or obese.

UNDERSTANDING THE CONNECTION

Every time a heart beats, it sends blood out into the body via the circulatory system. In between beats, the heart fills with blood. A person's blood pressure refers to two different but related measurements of this cycle. The first, known as systolic blood pressure, is the pressure inside the arteries when the

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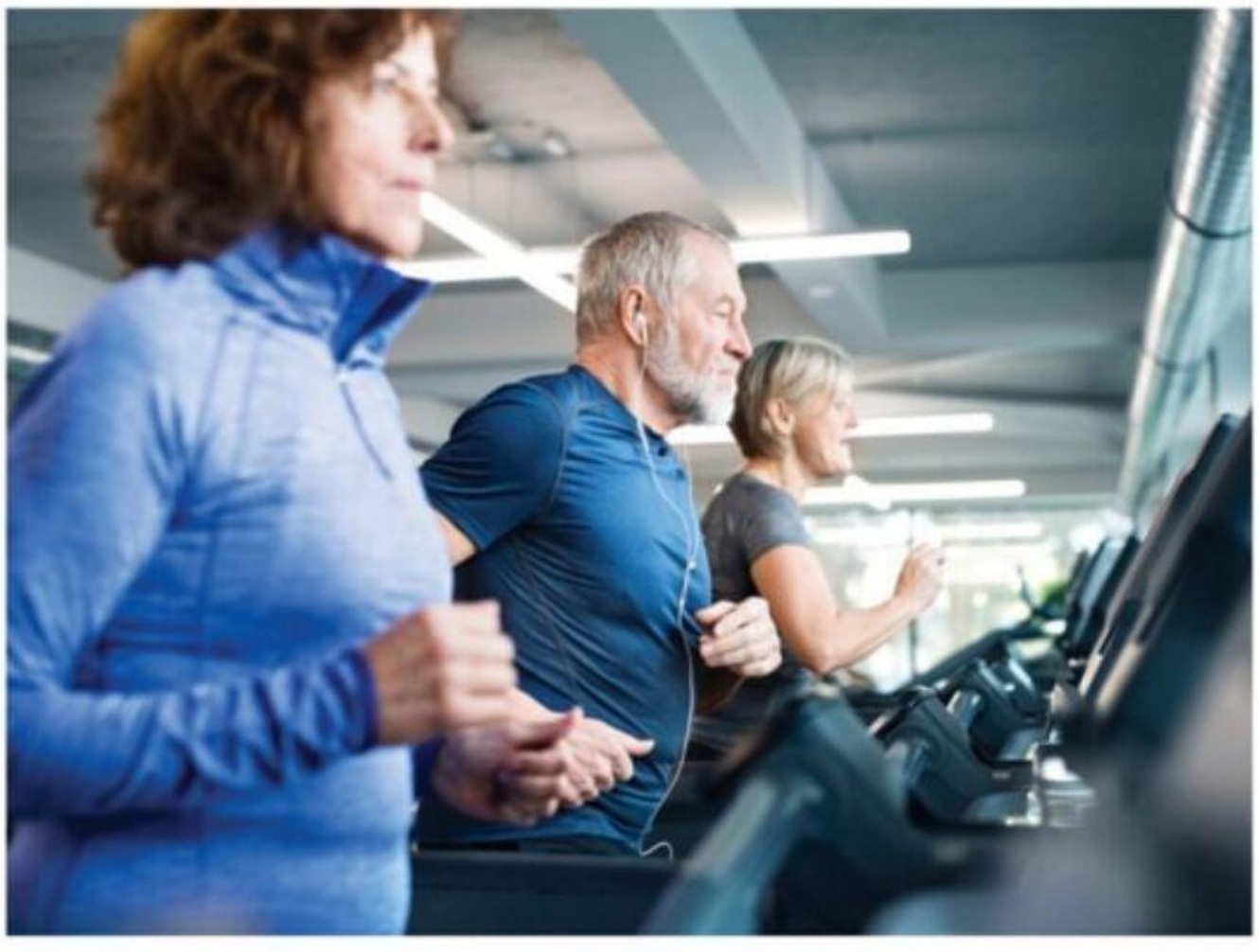
heart beats and pumps out blood. The second measurement, known as diastolic blood pressure, is the pressure inside the arteries when the heart is resting and filling with blood. These two numbers are usually presented together, and they almost always rise and fall in unison. In the United States, blood-pressure scores higher than 130/80 mm Hg are considered hypertensive.

Bakris says hypertension is often called a silent killer because it may present with no symptoms. Even when a person's blood pressure is dangerously high, the symptoms that develop are common and nonspecific—meaning they turn up for all sorts of reasons—so you may not connect them with high blood pressure. Dizziness, headaches, and blurry vision are among these nonspecific symptoms. By the time they set in, a person's blood pressure may have been elevated—and doing damage—for several years. What sort of damage? High blood pressure can stretch or injure your arteries in ways that raise your risk for heart disease, arterial disease, stroke, and other cardiovascular complications. High blood pressure also increases stress on the kidneys and some other organs.

Even if you're not exercising to lose weight, a workout routine can increase circulation and improve the function of small blood vessels, which can help lower blood pressure.



Type 2 diabetes is a medical condition defined by high blood-sugar levels. These high levels are caused by problems related to insulin, a hormone that signals to the body's cells that they need to absorb blood sugar. In people with type 2 diabetes, the cells become "resistant" to insulin, meaning they do not properly absorb blood sugar. As with hypertension, the early symptoms of type 2 diabetes—frequent urination, blurry vision, dramatic hunger spikes—may not raise immediate red flags. If someone isn't staying on top of their doctor's appointments, they may not be aware that one or both of these conditions is present.

How do type 2 diabetes and hypertension combine in ways that contribute to health problems? "Both affect the small blood vessels," says Dr. Mattias Brunstrom, a hypertension specialist and physician researcher at Umea University, in Sweden. "Diabetes affects the vessels in ways that make them stiffer, and high blood pressure impairs their function." This stacking of arterial damage helps explain why the combination of the two conditions is associated with cardiovascular problems, including higher rates of heart disease and stroke.

At the same time, both hypertension and type 2 diabetes may also promote higher than normal levels of blood sugar. Elevated blood sugar can damage the cells of the kidneys (as well as the heart and blood vessels). Kidney disease—and ultimately kidney failure—is a common complication among people with both of these conditions. "If you have [systolic] blood pressure consistently above 180, within 12 to 15 years, you will be on dialysis," Bakris says, referring to a medical procedure that removes, filters, and returns the blood to someone whose kidneys are no longer up to it. Elevated blood sugar caused by type 2 diabetes further damages kidney cells and increases the odds that the kidneys will struggle or fail to perform their job.

Although cardiovascular and renal problems are two of the most common complications, hypertension and type 2 diabetes can cause or contribute to a wide range of health problems—from dementia to blindness. "Both affect the vasculature, which can impair the health of any organ system," Brunstrom says.

Fortunately, there are effective ways to manage both conditions and therefore reduce all of these health risks.

WHAT YOU CAN DO

As is the case with most common health conditions, experts say that a combination of lifestyle changes and prescription drugs are often an effective one-two punch for people with both hypertension and type 2 diabetes.

"First, I would say that lifestyle changes are the basics of all disease management," Brunstrom says. He reemphasizes the strong associations that link hypertension and type 2 diabetes to obesity, and the role excess weight plays in exacerbating many health complications. "Obesity or overweight is a huge driver of both of these conditions, so weight management would be very crucial," he says. "Diet, exercise—any way you can get your weight down is good."

Even if you're not losing weight, exercise is still beneficial. "It increases circulation around the body and improves function of the small vessels, which might get [blood] pressure down," he says. "It might also improve the sensitivity to insulin and reduce glucose." That's all good stuff. Even short of sweaty exercise sessions, spending less time sitting or in a sedentary position—walking, for example, or doing chores around the house on your feet—may be helpful.

When it comes to eating, Brunstrom highlights the DASH diet, which is endorsed by the National Heart, Lung, and Blood Institute for the management of hypertension. (DASH stands for dietary approaches to stop hypertension.) The DASH diet involves limiting your intake of saturated fats, which are common in red meat and fatty dairy products, and cutting down on your intake of salt and sugary foods and drinks. Meanwhile, the DASH diet includes lots of fruits and vegetables. Recently, some researchers have examined the benefits of intermittent fasting plans for the management of type 2 diabetes. These approaches involve limiting or eliminating all caloric intake for an extended period of time, usually 16 hours or longer. There's evidence that intermittent fasting may be beneficial. It also appears to be safe for people with early or mild disease. "But if you have diabetes and are on medications, these diets can wreak havoc," Bakris says. "If you want to try that, you need the help of a physician or accredited diabetes dietitian."

Weight-loss surgery may be a treatment option worth considering. Recent research shows that bariatric surgery has helped both young people and adults get better control of their diabetes and hypertension. In some cases, especially those of teenagers, weight-loss surgery has removed the need for medications or even eliminated the diseases entirely. Patients should seek medical advice on whether the procedure is safe for them.

Apart from surgery and lifestyle interventions, experts agree that prescription medications are almost always necessary to manage these diseases. "You can reduce your pill burden if you're really good on the lifestyle side—so eating right, reducing sodium intake, exercising regularly," Bakris says. "But even on the low end, most people with diabetes and hypertension are going to require four to six medications." Adds Tom Brouwer, a cardiology resident and researcher at Amsterdam University Medical Centres, in the Netherlands: "I always compare [taking] them to doing your taxes or brushing your teeth. It's not fun, but you need to do it."

In the United States, medical guidelines recommend that people with both hypertension and diabetes reduce blood-pressure scores to below 130/80 mm Hg. There's some ongoing debate about whether targeting even lower numbers would be beneficial. Brouwer has conducted research in this area and says that, in many cases, he's a proponent of aiming for a systolic BP of 120. "If a patient tolerates it, I tend to try to lower their blood pressure all the way to 120," he says.

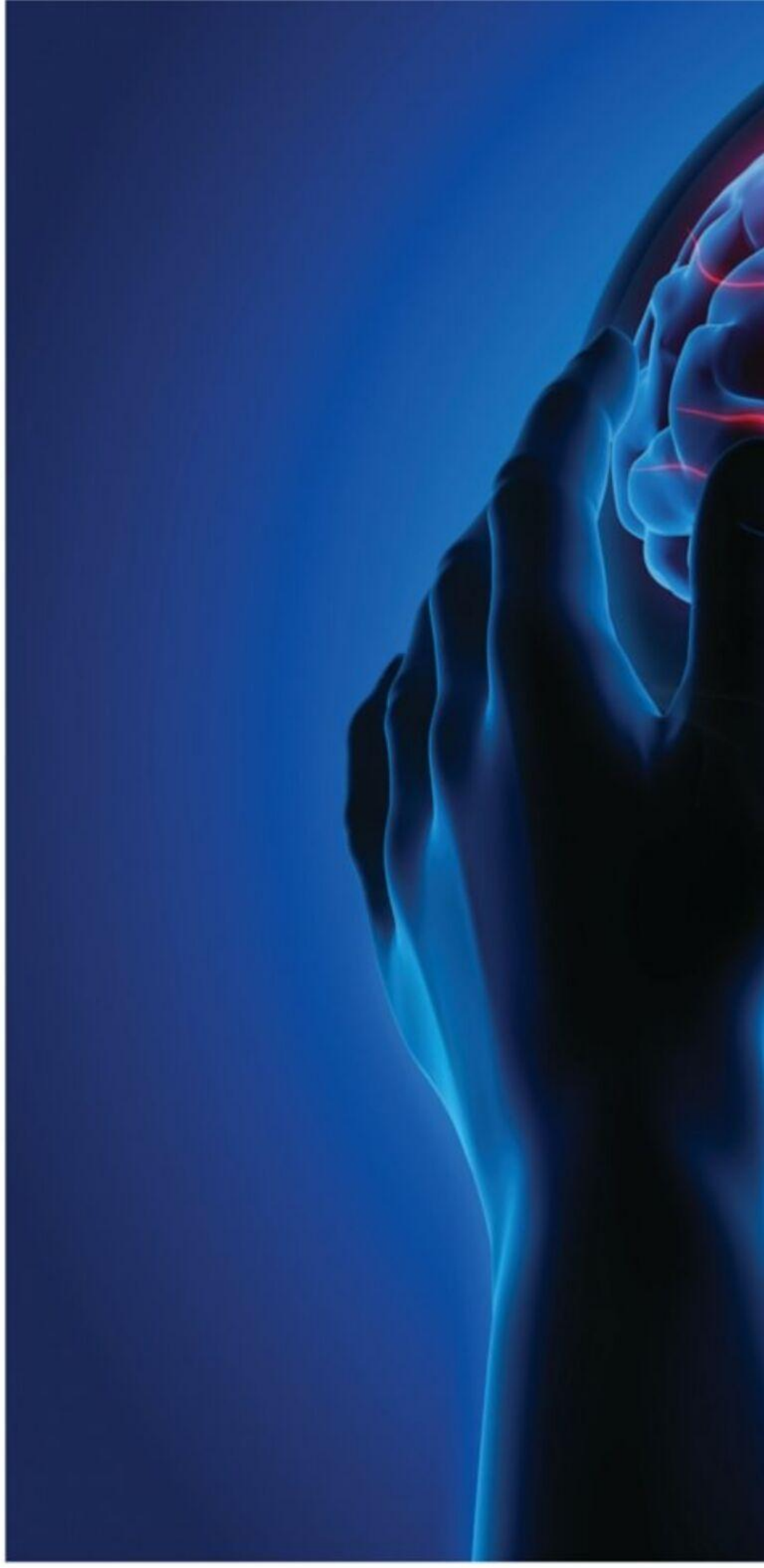
There are many different drugs used to treat people with hypertension and type 2 diabetes. But two of the most popular options are angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers, both of which help relax the arteries and thus assist blood flow. Apart from being effective for hypertension, these drugs also help protect the kidneys. Diuretics (drugs that increase urination), beta blockers, and calcium channel blockers are common treatments as well. "With these three drugs, an overwhelming majority of patients get to the target blood pressure," Brouwer says.

For those at risk for hypertension, diabetes, or both, experts say that the lifestyle measures outlined here—a good diet, exercise, and maintaining a healthy weight—are among the best ways to lower your risks. By following your doctors' drug recommendations and trying to live a healthier life, you can protect yourself from serious complications. "I tell patients: You can help yourself," Bakris says. "But you have to put in the effort." □

INCREASED ODDS FOR A STROKE

TOO MUCH GLUCOSE IN THE BLOOD COULD LEAD TO A RISE IN FATTY DEPOSITS IN THE BLOOD VESSELS. THE MOST EFFECTIVE TREATMENT: PREVENTION.

BY ELIZABETH MILLARD



AFTER SPENDING NEARLY TWO DECADES trying to manage her type 2 diabetes, Agnes Czuchlewski in 2015 found herself in the emergency room. The New Yorker was told she'd not only had a heart attack, she had metabolic syndrome—a cluster of conditions that includes diabetes and brings a higher risk of heart disease and stroke. "Because I needed to lose quite a bit of weight when I was first diagnosed, I was focused on the number I saw on the scale, and then on my blood-sugar numbers," recalls Czuchlewski, 70. "I didn't realize other numbers came into play, like blood pressure and cholesterol. That came as a shock."

Many people know that type 2 diabetes is a chronic, debilitating disease. What they might not realize is that it also increases the risk of a number of other conditions, including heart disease and stroke. In fact, people with diabetes have double the risk of stroke compared with those without diabetes, according to the American Heart Association (AHA). They also tend to develop heart disease or have a stroke at an earlier age. By the AHA's estimate, an American adult with diabetes is hospitalized for stroke every two minutes.

The connection is related to how the body handles blood glucose to make energy, says Dr. Deepak Gulati, a neurologist at the Ohio State University Wexner Medical Center's Comprehensive Stroke Center. When food is broken down into glucose, it uses the hormone insulin to enter cells, but those with type 1 diabetes lack the insulin needed for this process. With type 2 diabetes, too little insulin is

produced. In both cases, this can cause too much glucose to remain in the blood, which can result in increased fatty deposits in the blood vessels.

"These blood vessels are in the brain, heart, and other organs," says Gulati. "The deposits can weaken the walls of the blood vessels and also cause blockages, which significantly increases risk for heart attacks and stroke."

That doesn't mean cardiovascular problems are inevitable for those with diabetes. Although there are some factors you can't change, like family history or your age (stroke risk increases as you get older), the good news is that there are ways to make stroke prevention more robust when you have diabetes.

BE AWARE OF YOUR RISK LEVEL

The first step for prevention is simply to be aware of the link. Like Czuchlewski discovered, managing diabetes is crucial for health, but without knowing about stroke risk, you could be ignoring other essential variables like blood pressure and choles-

terol. "Often, we see patients who have their blood sugar at a good level, and their diabetes controlled, but they have no idea they need to focus more on cardiovascular health than someone without their condition," says Dr. Caroline Messer, an endocrinologist and medical director of the neuroendocrine center at Lenox Hill Hospital, in New York.

Awareness needs to go in both directions, she adds. Just as people with diabetes should understand stroke risk, those with cardiovascular issues should consider the possibility they have diabetes. Sometimes, Messer says, a person in the emergency room who's had a stroke or heart attack will be told they also have diabetes, and that can be alarming.

You don't need to wait for a dramatic health event. If you have other risk factors for heart disease like high blood pressure, sedentary habits, poor nutrition, and high cholesterol, Messer suggests a checkup that looks at the possibility of diabetes and heart issues, since they go hand in hand. "Risk for one can raise risk for the other," she says.

KNOW YOUR NUMBERS

With diabetes, the numbers that get the most attention are daily blood-sugar levels as well as the A1C—a test that measures blood-sugar levels over three months as a way to spot trends. But it's also important to understand where you are in terms of cholesterol and blood pressure. "High blood pressure, or hypertension, on its own doesn't have any symptoms, so people may not know it's a problem for them until they have an event like a stroke or heart attack," says Gulati. "As someone with diabetes, you should be very aware of what your blood-pressure reading is, given your higher stroke risk."

A normal blood pressure is 120/80 mm Hg, according to the U.S. Centers for Disease Control and Prevention (CDC). A reading of 140/90 or above means you have hypertension, which can damage arteries or cause them to burst or get blocked more easily. In the case of blockage, oxygen may have difficulty reaching or be unable to reach the brain, which could result in a stroke.

Similarly, high cholesterol usually has no symptoms. Without realizing it, you could have sky-high levels of low-density lipoprotein, or LDL (the "bad cholesterol,"), indicating fatty deposits in the blood vessels. These plaque deposits could narrow your arteries, causing your heart to pump harder to get blood through your body, which in turn increases blood pressure. For a person with diabetes (and depending on the number of risk factors the person has for heart disease) the optimal level of LDL cholesterol is less than 100 mg/dL. In terms of high-density cholesterol (HDL, often called the good cholesterol), 40 mg/dL is considered the optimal level for a person with diabetes or heart disease. HDL absorbs cholesterol, and higher levels of this lipoprotein can lower your risk for heart disease and stroke.

EXPAND YOUR CARE TEAM

Because of the high risk of stroke for those with diabetes, Messer suggests adding a cardiologist to your care team, in addition to an endocrinologist. "Everyone with diabetes should see a cardiologist at least once a year, especially if you have additional risk factors, like hypertension or family history of stroke," she says.

You may also want to consider health professionals with the expertise to address both heart health and diabetes, including a diabetes educator, a registered dietitian, a physical therapist, and, if you smoke, a smoking-cessation counselor. Quitting tobacco is key, since people with diabetes who smoke are 3.5 times more likely to have a stroke than those who don't, according to a 2018 study in the journal *BMJ Open*; people with diabetes who smoke can also damage their blood vessels and increase insulin resistance, according to a study that appeared in a 2009 edition of *Diabetes Care*.

CONSIDER MEDICATION IF RECOMMENDED

If you have high cholesterol or hypertension, your doctor may suggest medication that addresses those issues, such as calcium channel blockers or statins, says Gulati. Although a medication regimen will depend on your specific situation, Gulati adds that options like these are not only safe to take with diabetes medication, but that it's fairly common for them to be paired together.

Even if your numbers are in a good range, another option you and your doctor might consider is a diabetes drug class called GLP-1 agonists, says Messer. This class of medication has been shown to help with blood-sugar control and potential weight loss, and research indicates it's promising for decreasing risk of stroke in people with diabetes.

Whatever drug therapy you and your doctor decide to try, it is essential you adhere to your medi-

Quality sleep, lowering stress, quitting smoking, and maintaining social connections have been shown to help with blood pressure regulation.

cation schedule. That might sound obvious, but a 2014 study in *JAMA* found that medication nonadherence—when people don't take their meds as recommended—is a common problem, and up to half of adults in the U.S. who take prescriptions may struggle with it. Another study, about diabetes medications specifically, found that nonadherence is associated with poor glycemic control and higher risk of diabetes complications.

FOCUS ON HEART-HEALTHY LIFESTYLE CHANGES

Heart-boosting lifestyle habits are also key. For example, regular physical activity, quality sleep, lowering stress, quitting smoking, and maintaining meaningful social connections have been shown to help with factors like blood pressure regulation, says Dr. Jason Tarpley, director of the Stroke and Neurovascular Center for the Pacific Neuroscience Institute at Providence Saint John's Health Center, in Santa Monica.

Eating the proper amount and kinds of carbohydrates and fats, for example, is one of the most effective ways to control blood sugar. Consider some heart-healthy diets for inspiration, suggests Tarpley. "Food is pretty darn good as a starting point," he says. "An approach like the Mediterranean diet can help with both your diabetes and your cardiovascular health, particularly with its emphasis on seafood, beans, and nuts."

Similarly, regular exercise can improve blood-sugar control, contribute to weight loss, and even help with emotional well-being—and not enough sleep can have the opposite effect. Not only can too little sleep increase insulin resistance, but getting less than six hours of shut-eye a night can impact the regulation of hormones like cortisol and melatonin, which is particularly harmful for people with diabetes who already face hormone challenges.

"There are many factors you can't change when it comes to stroke risk as someone with diabetes," Tarpley adds. "You can't change your genes or your age, most notably. But there are modifiable factors that can make a huge difference. It's actually exciting to see how much better you can feel with habits like these, and you'll be lowering your risk of stroke at the same time." □

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Patient

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OZEMPIC: A POP CULTURE PHENOMENON

THE DRUG, DESIGNED TO TREAT DIABETES, IS NOW A POPULAR ANTI-OBESITY TREATMENT. BUT IS IT REINFORCING OLD, DAMAGING BODY STANDARDS ROOTED IN STIGMA, NOT SCIENCE?

BY JAMIE DUCHARME

IT'S UNUSUAL FOR A MEDICATION TO become a household name; even more uncommon for its branding to become, like Advil, shorthand for an entire class of products; and rarest of all, for it to change not just U.S. medicine, but U.S. culture.

Ozempic has done all three.

Approved in 2017 as a type 2 diabetes medication, Ozempic has largely made its name—and a fortune for its manufacturer, Novo Nordisk—as a weight-loss aid. Novo Nordisk knew early on that diabetes patients often lost weight on the drug, but even company executives couldn't have guessed how widely it would eventually take off as both an off-label anti-obesity treatment and a vanity-driven status symbol for those simply looking to shed a few pounds. Its runaway success mirrors that of similar medications, including Eli Lilly's Mounjaro and Wegovy, another Novo Nordisk product and the only one in the trio technically approved for weight loss. Prescriptions for all of them are flying off the pad at an eye-popping rate.

Novo Nordisk sold around $41 billion's worth of its various diabetes and obesity drugs in 2024, and Eli Lilly sold more than $12 billion's worth of Mounjaro. Prescriptions for these weight-loss medications close to doubled between July 2017 and February 2024; one in every 20 prescriptions written for adults in the United States last year was for a GLP-1 drug, according to statistics from the Massachusetts Institute of Technology. Demand at one point was so great that there were shortages of Ozempic, Wegovy, and Mounjaro, and patients with type 2 diabetes sometimes struggled to fill their prescriptions as they competed for limited supplies with people looking to slim down. Those shortages have resolved, according to the FDA, with sales of a number of GLP-1 drugs slowing, even as an increasing number of players—spas, internet suppliers, weight-loss companies, and compounding pharmacies—compete for a piece of the GLP-1 pie.

No one can quite agree on whether this frenzy is a good thing. Plenty of physicians (and of course the pharmaceutical executives who stand to get very, very rich) say it is, given that roughly three quarters of U.S. adults qualify as either overweight or obese and are thus, according to leading public-health authorities, at risk of a range of serious health complications. "Obesity is an epidemic, and we urgently need effective treatments," says Dr. Sahar Takkouche, an obesity and bariatric medicine specialist at Vanderbilt Health.

But some doctors, researchers, and activists are uneasy about living in the age of Ozempic—one that has felt like a kind of déjà vu, a return to an era when thinness and weight loss were unquestioningly valued. Before the Ozempic tsunami, a growing number of doctors and researchers had begun advocating for Health at Every Size, a research-backed set of principles from the Association for Size Diversity and Health that hold that all people deserve high-quality, nonstigmatizing medical care. Their efforts contributed to a burgeoning field known as "weight-neutral" medicine, which sees "weight" and "health" as separate, and worked in tandem with the wider body-positivity movement to help loosen the diet industry's grip on American psyches. As the 2000s progressed, women's magazines stopped pushing diets quite so hard. Clothing brands bragged about hiring models larger than size 0. Even Weight Watchers rebranded as a "wellness" company called WW.

Then Ozempic and its cohort came along, and it turned out lots of people still wanted to be skinny. Some industry watchers have even predicted that the rise of drugs like Ozempic—and an impending crop of new, potentially more effective competitors—could spell the end of obesity. But as these drugs transform both standard medical practice and cultural ideas about weight loss, a contentious debate is simmering: Should we even be treating obesity?

The U.S. medical establishment is clear about its stance on obesity: It is a "common, serious, and costly chronic disease," as the U.S. Centers for Disease Control and Prevention put it. By CDC estimates, more than 40 percent of U.S. adults and almost 20 percent of children and adolescents are obese, putting them at risk of health problems including heart disease, type 2 diabetes, stroke, and certain cancers. An additional 30 percent of adults are considered overweight, meaning less than a third of U.S. adults meet the CDC's standard for a healthy body weight.

If obesity is a disease, it follows that it should be treated. Historically, diet and exercise have been plan A for treating obesity. But in practice, lifestyle changes often aren't enough. "Try as we might, a lot of exercise typically does not result in a significant amount of weight loss," says Glenn Gaesser, a professor of exercise physiology at Arizona State University. That's in part because people tend to get hungrier the more they move, offsetting whatever calories they burn at the gym, and in part because the body gets used to its size and works to stay at that set point, Gaesser explains. Lifestyle fixes can work for some, studies show, but lots of people lose only modest amounts of weight or regain the pounds over time—a process known as "weight cycling," which is itself linked to cardiovascular and metabolic health problems.

For years, doctors had relatively few options to offer the many patients for whom diet and exercise didn't work—treatments like the type 2 diabetes drug metformin, which can cause a modest amount of weight loss, and bariatric surgery, which works well but is unpopular among patients. And then came Ozempic and the rest.

Ozempic, Wegovy, and Mounjaro all work by simultaneously slowing digestion and mimicking the appetite-suppressing hormone GLP-1, through a weekly injection. This double whammy means people need to eat far less food than usual, leading to an average 15 percent to 20 percent reduction in body weight after about a year. These drugs don't work well for everyone, but compared to older meds "the

Ozempic, Wegovy, and Mounjaro slow digestion and mimic an appetite-supressing hormone.

efficacy of these drugs is remarkable," Takkouche says. "The weight loss is undeniable." And this class of drugs doesn't just lower the readings on a scale. According to data from Novo Nordisk, semaglutide (the generic name for both Ozempic and Wegovy) slashes the risk for major cardiovascular events like heart attack and stroke by 20 percent among overweight or obese adults with heart disease.

Justin, who asked that only his first name be used to protect his privacy, saw "life-changing" results when he began taking Wegovy in 2023. After struggling to lose weight through diet and exercise, the 30-year-old from North Carolina lost about 30 pounds in less than six months on the medication. As he followed instructions and scaled up his dosage over time, though, Justin started to experience side effects including acid reflux, nausea, diarrhea, and lethargy. Eventually, Justin felt he had to choose between his health and his quality of life. As much as it pained him, quality of life won out.

Six months after quitting Wegovy, Justin had gained back about half the weight he had lost, a common outcome for patients who stop using GLP-1 drugs—which many do, either because of side effects or cost, since many insurance plans don't cover weight-loss drugs and out-of-pocket prices can exceed $1,000 a month. Despite his mixed experience, Justin would still recommend that someone trying to lose weight consider Wegovy, and he may someday go back on it himself at a lower dose. "It made enough of a difference, and it's something I've been wanting for so long" that it's tempting to go back, he says.

Many obesity-medicine specialists share Justin's feelings. "We have effective tools" for weight loss now, says Dr. Laura Davisson, director of medical weight management at West Virginia University Medicine. "Why not use them?"

There is one big reason, according to a passionate group of doctors, researchers, and activists who believe in the principles of Health at Every Size. They feel obesity never should have been labeled a disease in the first place—and thus may not need to be treated at all. "Manipulating weight is not a path to health," says Ragen Chastain, a certified patient advocate who coauthored a library of Health at Every Size resources. "The belief that fewer fat people existing is good—that's weight stigma."

As Chastain and others like her see it, Ozempic and its sister drugs are not lifesaving anti-obesity medications, but new tools for reinforcing old, damaging body standards rooted in stigma, not science—all while raking in gobs of money for pharmaceutical companies.

The idea that obesity is not a disease is still a controversial take in mainstream medicine. The CDC and the American Medical Association (AMA) disagree with it, as do many physicians in the field. "'Healthy at any size'—I don't even like the connotation," says Dr. Caroline Apovian, codirector of the Center for Weight Management and Wellness at Boston's Brigham and Women's Hospital.

And yet, the research on weight and health leaves room for questions. There are plenty of studies that show links between obesity and health problems, ranging from fatty liver and sleep apnea to heart disease and cancer. But studies also suggest that up to half of people with obesity are metabolically healthy, that people in that camp are not at elevated risk for heart disease and death, and that people who are overweight may in fact have a lower risk of premature death than people at "normal" weight. Studies have also found that, even though obesity is considered a risk factor for developing heart disease, overweight patients tend to fare better than thinner patients when they're treated for related conditions, a finding often called the "obesity paradox."

"We've got this entire body of research based on a hypothesis that if you make fat people look like thin people they'll have the same health outcomes," Chastain says. But she's not convinced that's the case at all.

For one thing, body mass index (BMI), the measure commonly used to diagnose overweight and obesity, is inherently flawed. In fact, when the AMA designated obesity a disease in 2013, its own Council on Science and Public Health urged against the designation. The council's chief concern was the imprecision of BMI, a crude measure of total weight relative to height that, on its own, does not say much at all about someone's health. It does not, for example, distinguish between fat and muscle.

BMI's path to ubiquity is convoluted. The formula—weight in kilograms divided by height in meters, squared—was developed in the 1830s by Adolphe Quetelet, a Belgian mathematician interested not in diagnosing obesity, but in defining the "average man," an effort that mostly glossed over people other than White men. The resulting formula, known as the Quetelet Index, fit neatly into the burgeoning field of "race science," a pseudoscientific

effort to draw distinctions between people of different races that fed into the eugenics movement, explains scholar Sabrina Strings, author of *Fearing the Black Body: The Racial Origins of Fat Phobia.*

By the early 1900s, prominent U.S. eugenicists had latched on to the idea that fatness was a marker of moral failing associated with people of color. "We think that fatness is linked to disease," Strings says, but "the history of fat stigma actually transits through race science and eugenics."

Later, in the 1960s, Black women were integral in starting fat-liberation movements that laid the groundwork for the modern body-positivity movement. These activists ran counter to the mainstream medical community, which was growing increasingly concerned about weight. In the 1970s, more than a century after the Quetelet Index was first developed, the prominent American physiologist Ancel Keys revived it. Keys felt insurance companies were using flawed methods of assessing weight-related health risks among people they covered. He proposed using the Quetelet Index (renamed BMI) instead—even though, in a study he coauthored in 1972, Keys did not demonstrate that BMI consistently correlated with future heart disease risk.

Today, experts widely agree that BMI is imperfect. And yet, it's still used in research, to diagnose obesity, and to determine who is eligible for drugs like Wegovy. "We're knowingly saying, 'We don't even know how to measure [excess fat], but we're going to use the measure we have anyway and define two thirds of the population as diseased,'" says Dr. Lisa Erlanger, a Seattle-based family-medicine physician who supports Health at Every Size.

Erlanger believes that weight functions less as a measure of health than as a social determinant of health—in other words, a nonmedical factor that nonetheless affects health through its impact on overall wellness. The weight stigma larger people encounter in doctor's offices, the workplace, and social settings can all harm health, Erlanger says. And in the United States, adults with obesity are likely to be non-White and non-college-educated, two socioeconomic factors also linked to poorer health outcomes due to structural inequality.

Erlanger feels so strongly that she has stripped weight from her medical practice wherever possible. Her office is designed to be comfortably navigated by people who are larger. The reading material in the waiting room doesn't mention diets or weight loss. She doesn't weigh patients at the beginning of their appointments. She never prescribes weight loss, and especially not weight-loss drugs. "I support anyone's efforts to reduce their marginalization in society," she says. But, at the same time, "I believe I have an ethical obligation not to offer a treatment with false promises."

It wasn't weight loss that motivated Irene, who is 55 and lives in Washington State, to ask for a semaglutide prescription. Irene—who asked to have only her first name used to preserve her privacy—has binge-eating disorder and often stayed up late into the night, snacking for hours after her family had gone to bed. Irene read on social media that semaglutide had helped other people manage their binge-eating disorder, so it seemed worth a try. But it also felt something like self-betrayal.

For most of her life, Irene had been locked in a cycle of losing and regaining weight, obsessing about food and calories. Then, a few years ago, she learned about Health at Every Size and threw herself into the community with gusto. She sought out doctors who shared her perspective and joined a fat-liberation group—which made her deeply hesitant about using semaglutide, a drug infamous for helping already skinny Hollywood starlets slim down. "It has been tricky to lose some weight and not get caught up in that as an aspiration going forward," Irene says.

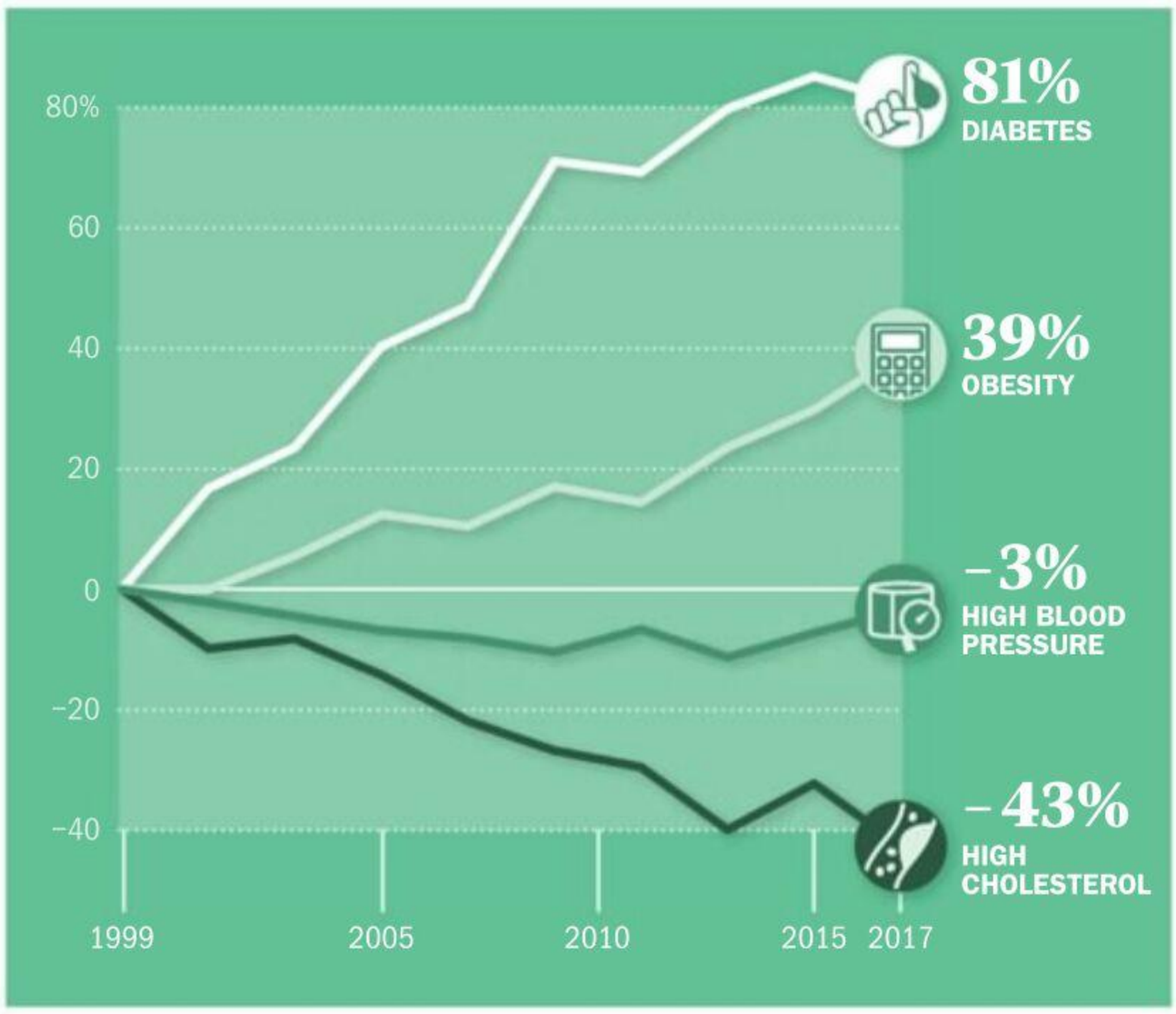
But now, she has to balance her support for the movement with the reality that, in an effort to manage her eating disorder, she has become one of the millions of people driving demand for anti-obesity medications to new heights.

The landscape for pharmaceutical companies has grown increasingly competitive. While some industry watchers have predicted that Mounjaro could eventually generate $50 billion a year in annual sales, making it one of the highest-selling drugs of all time, growth has slowed for maker Eli Lilly, and Novo Nordisk's market capitalization has skidded, falling from $442 billion in October 2024 to $315 billion in July 2025.

At the same time, an army of new weight-loss medications are receiving or marching toward regulatory approval, some with results even more impressive than their predecessors. Data from Eli Lilly suggest that tirzepatide, the active ingredient in two dual GLP-1/GIP receptor agonists, Mounjaro and Zepbound, can help people lose about a quarter of their body weight in less than two years. The pharma giant, along with some of its competitors, is exploring oral GLP-1 drugs, and the first is expected to make it to

MEASURING HEALTH

Diagnosis rates for diabetes and obesity (determined by BMI) have grown significantly, while those for high blood pressure and high cholesterol have fallen. At right, the change in diagnosis rates over time.



SOURCE: CDC; TIME GRAPHIC BY ELIJAH WOLFSON

market by the end of 2025. Oral forms would have an even lower barrier to entry than their injectable formulas. (Novo Nordisk's Rybelsus is already available as a pill.) With so many options currently or soon to be available, it's not so far-fetched to imagine a world where all anyone needs to lose weight is a prescription.

Davisson, the obesity specialist from West Virginia, says that roughly 80 percent of her patients are already on some form of weight-loss drug. She feels anyone who is overweight or obese should consider some form of treatment, since they may develop complications over time even if they're healthy at the moment. "Everyone is metabolically healthy," she says, "until they're not."

But other physicians are struggling with their place in this new world. When Dr. Mara Gordon, a family physician in New Jersey, finished her medical training a decade ago, she didn't question the idea that weight loss was a good thing. But the longer she practiced—and saw how patients shut down when she urged them to drop a few pounds—and the more studies she read, the more she began to doubt whether weight loss should be an assumed goal. "I found, increasingly, that it was all downside," she says.

Gordon minimized weight's role in her practice, focusing instead on other markers of health—things like insulin resistance (which can predict diabetes risk), blood pressure, chronic pain, mental health, and quality of life. Today, though, more and more patients come into her office asking for Ozempic and Wegovy by name. Often, she says, patients who want to drop pounds are technically overweight but have little medical reason for taking a GLP-1 drug: normal cholesterol, good blood pressure, no diabetes or warning signs for it. On a purely medical basis, Gordon feels there's no need to take out her prescription pad.

But when she looks at the whole picture, the decision becomes more complex. Her patients' test results may not signal a problem, but they're still desperate to lose weight—maybe so they have the energy and mobility to play with their kids or to improve their body image or simply fit into a world that prizes thinness. In those moments, Gordon has to set aside her personal feelings about Ozempic and about weight loss writ large.

"If you're facing hatred and fat phobia on a daily basis, if you can't do the things you need to do because the chair at your office isn't the correct size," Ozempic may truly help, Gordon says. "I wish we lived in a less superficial society. But my job is to take care of the patient right in front of me."

She often writes the prescription in the end. ◻

CHAPTER 3

MANAGING YOUR DIABETES

IF YOU ARE LIVING WITH TYPE 2 DIABETES, KEY TOOLS INCLUDE A HEALTHY DIET, REGULAR EXERCISE, AND GOOD SLEEP.

THE HOLY GRAIL: TYPE 2 DIABETES REMISSION

LOWERING YOUR A1C TO A HEALTHY LEVEL AND KEEPING IT THERE FOR THREE MONTHS—WITHOUT MEDICATION—IS POSSIBLE, BUT IT DOESN'T MEAN YOU'RE CURED OF THE DISEASE.

BY MICHAEL O. SCHROEDER

TYPE 2 DIABETES NEARLY KILLED Anthony Wilson before he had even been diagnosed.

One morning in 2012, Wilson's wife, Sheila, woke up for work, and she saw that her husband had dark circles under his eyes and his skin looked gray. She knew something was seriously wrong and that she had to get him to the hospital immediately. He resisted, but she persisted and prevailed, he recalls.

"She walked me down the stairs at home, and the next thing I remember was when I woke up in the ICU," says Wilson, an EMS operations manager now in his mid-50s who lives in Virginia Beach, Virginia. Tests revealed that Wilson's blood sugar was multiple times higher than the threshold needed to diagnose type 2 diabetes, a chronic condition in which the body doesn't use insulin properly, allowing blood sugar to rise unchecked.

So intense was the strain on Wilson's body that his organs were failing. His doctors were talking about putting him on dialysis because of kidney failure, and they had to shock his heart twice to get it back into rhythm because his diabetes had exacerbated an underlying heart condition, Wilson says.

Once he was stabilized, a doctor told Wilson he had type 2 diabetes and would need to take insulin for the rest of his life. But not only was he able to come off insulin within months of his diagnosis, he now also can keep his blood sugar in a normal, healthy range with no diabetes medication at all.

After losing 60 pounds in 2020—thanks to diet changes and regular exercise—Wilson, a volunteer for the American Diabetes Association (ADA), achieved what's considered the holy grail in type 2 diabetes management, by bringing his condition into so-called remission, meaning the person has a blood-sugar level below the established threshold for a diabetic diagnosis for at least three months, without taking diabetes medications. That would be below, for example, a 6.5 percent measurement of the A1c, the blood test that's used to get a three-month average of blood sugar.

"I'm the type of person who wants to be in control of my health," says Wilson, who continues to be

The more time that passes after a diabetes diagnosis, the harder it becomes to lower blood sugar to below diabetic levels without medication.

vigilant about monitoring his blood sugar. "I share my story with anybody who will listen, in hopes that it can make a difference."

DIABETES 'REVERSAL' BY ANOTHER NAME

The concept of type 2 diabetes remission, which is getting increasing attention from researchers and doctors, also goes by other names, including diabetes "reversal," "resolution," and even "cure." But a consensus of experts led by the ADA in 2021 agreed on the term *remission* as being most accurate."The reason we use the word *remission* is because if someone were to think that they were cured or reversed, the challenge is they may then not feel like they need to have anything checked," says Dr. Robert Gabbay, ADA's chief science and medical officer.

A healthy diet is one way to improve the chance of remission.

WEIGHT LOSS CAN CUT FAT LEVELS INSIDE THE LIVER AND PANCREAS, LETTING THOSE ORGANS FUNCTION NORMALLY AND ALLOWING THEM TO BETTER REGULATE BLOOD-GLUCOSE LEVELS.

But a lot still remains unclear, such as how long remission generally lasts, because it varies. And experts stress that continued follow-up with health care providers—not only to monitor blood glucose but also to check for diabetes complications—is important, because the impact of diabetes remission (fleeting or long-lasting) on things like heart health and death rate isn't yet well understood.

Something to strive for, or a rare phenomenon?

Advances in the treatment of type 2 diabetes may put remission within reach for more people with the disease, especially those who have been more recently diagnosed. "The most common place we see [diabetes remission] is with bariatric surgery where there's significant weight loss," Gabbay says. In addition to the pounds dropped, there may be secretion of hormones as a result of the surgical reconfiguration of the gastrointestinal tract that makes remission more likely. Some research suggests that after gastric-bypass surgery is performed, certain gut hormones stimulate the production of insulin in the body, including the hormones glucagon-like peptide-1 (GLP-1) and peptide tyrosine-tyrosine (PYY), which drive down blood-sugar levels.

But while remission is strongly associated with bariatric surgery, research shows that significant weight loss alone—without surgery—can be enough to put type 2 diabetes into remission. A closer look reveals that weight loss can cut fat levels inside the liver and pancreas, letting those organs function normally and

allowing them to better regulate blood-glucose levels.

And remission isn't accessible to just a select few. The DiRECT trial published in the *Lancet* in 2018 found that nearly half (46 percent) of 149 participants studied—who had been diagnosed with type 2 diabetes within six years and who weren't on insulin—were able to achieve remission through an evidence-based weight-loss program. The research was carried out in primary-care practices—not specialized weight-loss centers—over a period of a year. Those who lost 33 pounds or more were most likely to achieve remission. A third of participants remained in remission at the two-year mark, according to research published in *Lancet Diabetes & Endocrinology*, with sustained remission linked to keeping the weight off.

The biggest factor in whether a person can lower blood sugar below diabetic levels and keep it there without medication is the amount of time that has passed since diagnosis, according to Dr. Roy Taylor, professor of medicine and metabolism at the Translational and Clinical Research Institute at Newcastle University upon Tyne, in the U.K. Taylor was the co–chief investigator and co–senior author of the DiRECT trial.

Despite study results like those from the DiRECT trial, to Taylor's frustration, many doctors contend that such weight loss is difficult for patients to achieve and then maintain. They stress that diabetes control—not remission—remains a primary goal. It's very challenging for people to lose the amount of weight necessary to achieve remission, says Dr. Jill Crandall, professor of medicine and chief of endocrinology at the Albert Einstein College of Medicine and Montefiore Health System, in New York City. "It may be that we're overlooking an opportunity to really motivate patients for that weight loss by introducing the notion of remission. But I think it's not first in the mind of most clinicians who are treating people with diabetes."

Others say it should be. "I used to feel like I was handing out a life sentence when I diagnosed a patient with diabetes. I now work with my patients to reverse their disease," says Dr. Stephenie Lucas, an endocrinologist at Beaumont Health, which is based in the Detroit area. "Many patients with type 2 diabetes can go into remission and not require medication to maintain normal glucose levels."

One thing that's more universally accepted: Regardless of whether a patient is in remission, continued vigilance is key. "There is no permanent cure for diabetes, because the cells that produce insulin have been damaged and the underlying genetic factors remain," Lucas says. "The patient does maintain an increased susceptibility to recurrence of diabetes, so lifestyle interventions must be continued."

GIVING PATIENTS A CHOICE

Doctors stress that patients should be supported in making diabetes management a priority—however they choose to do so—regardless of whether the aim is remission. Prioritizing blood sugar control might mean some patients will continue to need lifelong medication, including insulin, says Dr. Gwendolyne Jack, endocrinologist and clinician-educator at Weill Cornell Medicine in New York City. "That's okay. That is not a failure on their part," she says.

But the impact of a diagnosis on patients—and the desire many patients have to control blood sugar without medication or insulin—shouldn't be ignored, Taylor and others emphasize. Survey results published in *Diabetic Medicine* in February 2018 show that the primary questions patients want researchers to answer about the disease are, Can type 2 diabetes be cured or reversed, what is the best way to achieve this, and is there a point beyond which the condition can't be reversed?

Taylor acknowledges that many people with the chronic condition see it as something the doctor will deal with; patients often get help with controlling blood sugar, but their goal isn't remission. "However, at least 40 percent of people with type 2 diabetes hate their condition and would go to lengths to get rid of it," he says. "They describe the moment of diagnosis as a hammer blow. Many doctors do not understand that."

For those who wish to work toward remission, Taylor suggests leaning into that motivation:

Write down your reasons, so you can come back to them later.

Discuss your plans with those you live, work, and socialize with, to gain support and understanding.

Once you're ready, decide when to start—and prepare meticulously. "This is not a crash diet," Taylor says.

Understand that your chances of remission are best the closer you are to diagnosis, but it's still possible even up to 10 years after diagnosis. It's less common beyond that; waiting makes the goal harder to attain.

Many people with the chronic condition see it as something the doctor will deal with; patients often get help controlling blood sugar, and their goal is not remission.

Weight loss and maintenance, diet adherence, and activity are key to improving chances of remission.

Whether your aim is remission or to improve blood-sugar control through lifestyle changes in addition to taking diabetes medication or using insulin, you'll want to make it clear to your endocrinologist. And together, carefully parse out a dietary approach in advance of implementing changes to what you eat to ensure it's safe and that you're getting all the nutrients you need.

Since Anthony Wilson had other conditions that diabetes can exacerbate—including high blood pressure and supraventricular tachycardia, for which he needs a pacemaker, and a family history of kidney disease—it was it important to him to have a physician dedicated to the same treatment goals. When he went to his endocrinologist in 2020, they agreed Wilson should go on a strict 1,200-calorie-per-day diet. He ate lean proteins, drank plenty of water, limited carbs, cut sugar, decreased serving sizes, and stayed active. The plan, like other low-calorie and low-carb diets that can help increase chances of remission, led to a drop of 60 pounds, and Wilson continues to dedicate himself keeping his A1c well under 6.5 percent—the normal, healthy range.

Wilson credits his wife with supporting him throughout his journey. She exercises with him and helps him maintain a healthy diet. "We still have to hold each other accountable," says Wilson, adding that he uses the ADA as a resource and volunteers with the organization to support others. "I feel pretty good knowing that with hard work, you can accomplish a goal, and I've done that with the help of my family."

He's also careful not to grow complacent. That's something experts say is critical to not only achieving but, more important, maintaining type 2 diabetes remission. "I didn't work this hard to lose the weight to go back to the way it was," he says. ◻

LOWER YOUR CHOLESTEROL NATURALLY

DIABETES DAMAGES THE LINING OF YOUR ARTERIES, SO IT IS EASIER FOR CHOLESTEROL TO STICK TO THEM, BUT LIFESTYLE CHANGES CAN HELP LOWER YOUR RISK FOR DISEASE.

BY MARKHAM HEID

IN THE YEARS FOLLOWING WORLD WAR II, physicians in the United States and Europe noticed a surprising phenomenon: rates of heart attack and stroke fell dramatically in many places. Autopsies from this period also revealed reduced rates of atherosclerosis, a buildup of fatty arterial plaques that causes cardiovascular disease.

At first, experts were perplexed. But as time passed, many concluded that wartime food deprivations and the forced shifts in people's diets—namely, big reductions in the consumption of red meat and other animal products—contributed to the heart-health improvements. Later work, particularly the famous Framingham Heart Study, helped establish that blood cholesterol levels, driven in large part by a person's diet, tended to overlap closely with cardiovascular disease.

The idea that the foods a person eats could raise or lower the risk of unhealthy cholesterol levels and disease was, at first, a radical and controversial one. While there's ongoing debate about the relationship between red meat and poor health, the links connecting diet, cholesterol, and cardiovascular disease are beyond doubt.

Cholesterol is a waxy compound that your body uses primarily to make hormones and to firm up the walls of cells. "Our body needs some cholesterol for day-to-day functioning, but the amount our body needs is relatively small," says Dr. Laurence Sperling, the founder and director of the Heart Disease Prevention Center at Emory University, in Atlanta.

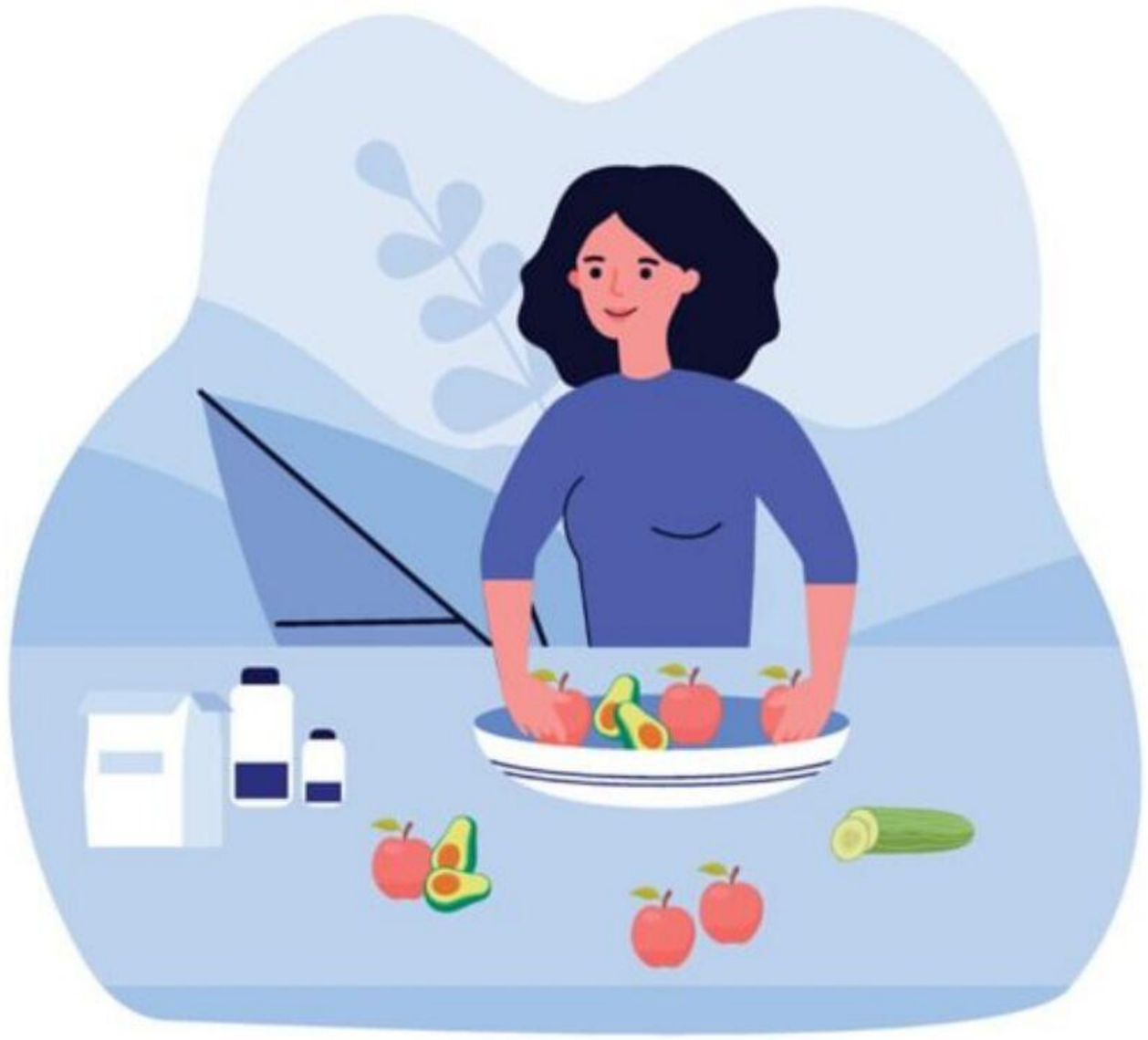
Different parts of the body, including the brain and the blood, contain cholesterol. It's the oversupply of cholesterol in blood that causes problems—

specifically, low-density lipoprotein (LDL), also known as bad cholesterol. Too much LDL in the arteries can "form a fatty streak, which is the precursor of atherosclerotic plaque," explains Dr. Francine Welty, a cardiologist at Beth Israel Deaconess Medical Center in Boston and former chair of the American Heart Association's lipid committee. LDL, therefore, is the primary building block of arterial plaque.

The two primary diseases associated with clogged arteries—coronary artery disease and cerebrovascular disease—are in fact two of the top three causes of death worldwide. More than one in four deaths are caused by one of these two conditions, and managing or lowering your blood cholesterol levels is a proven way to prevent these diseases. Sperling says ideal cholesterol levels vary depending on a person's age, sex, and health status. But, optimally, you want to keep your LDL below 70 milligrams per deciliter, the common measure used in the U.S. While drugs can help—and in some cases may be necessary—non-pharmacological approaches are just as important. "Lifestyle and behavioral approaches are the foundation of cardiovascular prevention for all," he says.

Here, experts detail effective lifestyle changes

that can help lower cholesterol. A proper diet, they all agree, tops the list.



HOW TO EAT TO LOWER YOUR CHOLESTEROL

One of the biggest trends in diet and nutrition advice is a movement away from talking about specific micronutrients and optimal daily servings of this or that food group. Instead, nutrition experts now talk a lot more about broad patterns of healthy eating. This means limiting certain foods while prioritizing others, rather than trying to hit narrow targets. "Something I tell a lot of my patients is that the Greek derivation of diet is *diaeta*, which means 'a way of life,'" Sperling says. "Dieting shouldn't be torture, or something you maintain for a month. It should be a meaningful and purposeful change you can extend throughout your life."

In this spirit, he says, one of the most important changes you can make is to pack your meals with lots of fresh fruits, vegetables, nuts, and whole grains. Many of the most effective and evidence-backed cholesterol-lowering eating plans—like the Mediterranean diet—prioritize these foods, he says.

Meanwhile, reducing your intake of animal products—especially red meat and processed dairy foods—is a move that research has repeatedly tied to cholesterol improvements. "I've run the lipid prevention clinic at my hospital for 31 years, and the first thing we tell people is to lower their intake of saturated fats," Welty says. She mentions red meat, butter, and dairy as foods people should aim to cut down on—not eliminate necessarily, but reduce—if they want to improve their cholesterol levels. Many Americans consume saturated fats, from eggs, dairy products, and red meat, with almost every meal. This sort of immoderation is a problem. "The Japanese have some of the lowest rates of cardiovascular disease in the world, and that may be because they eat much less red meat and saturated fat than we do in America," Welty says.

It's worth noting that saturated fat is a controversial topic in nutrition research. Some experts have argued that saturated fats get blamed for health problems that are likely caused by processed meats, refined carbohydrates (like those found in sugary or packaged foods), and the trans fats in fast foods and some packaged snacks. Others have argued that if people avoid meat and dairy but end up eating more processed or refined carbs, that's an unhealthy trade. On the other hand, experts generally agree that trading saturated fats for some of the healthy foods mentioned above—fruits, vegetables, and nuts—is a highly effective way to improve cholesterol scores and heart health. "If you decrease the saturated fat in your diet, that's one of the best ways to lower LDL," Welty says.

She adds that protein-rich soy-based products—from tofu to soy milks and yogurts—may also be good substitutes for meat, butter, milk, and other conventional saturated fat sources. "People in America are fixated on protein, but Americans don't really like to eat soy products," she says. This is unfortunate because research stretching back several decades has linked soy to improved heart health and lower blood cholesterol levels. "If you need to replace saturated fats with other proteins, soy would be a good option," she says.

Exchanging foods with hooves for foods with feathers or flippers is another good idea. "Replacing red meat and pork with fish and chicken is something we often recommend," Welty says. In particu-

lar, fatty fish, such as salmon, mackerel, and herring, are heart-healthy choices.

On the other hand, experts say fish oil—a popular health supplement—is not a helpful addition to your regimen. "Fish oil does not lower bad cholesterol," says Dr. Leslie Cho, director of the Cleveland Clinic's Women's Cardiovascular Center. She says that some prescription fish oil supplements can help lower triglycerides, a type of blood fat linked with cardiovascular problems, so doctors sometimes recommend them. But commercial fish oil supplements have been linked to an increased risk for abnormal heart rhythms and should be avoided.

Last but not least, Cho says that getting plenty of fiber in your diet—something most Americans fail to do—is extremely important. "Fiber can bind to dietary cholesterol and eliminate it from the body," she says. "We want you to aim for 25 grams of soluble fiber per day." This is possible if you're eating a lot of whole vegetables, fruits, and healthy whole grains, like oatmeal or flaxseed. But supplements can also help you get there. Cho says ground psyllium seed—sold under the brand name Metamucil and also in less expensive (but identical) generic products—is a helpful source of soluble fiber that can reduce your LDL levels.

NONDIET APPROACHES TO IMPROVING CHOLESTEROL

While lowering your LDL scores should be your primary focus, improving your levels of high-density lipoprotein (HDL) cholesterol—also known as the "good" kind of cholesterol—is also important. "HDL sucks cholesterol from blood vessels like a vacuum," Cho explains.

Exercise is one way to pump up your HDL levels. "It can raise your good cholesterol and also lower triglycerides," Sperling says.

However, when it comes to the best type of exercise for your cholesterol, the research is all over the place. One review of studies, published in 2020 in the journal *Systematic Review*, found that yoga has the strongest evidence in favor of its cholesterol-improving benefits. While many other types of exercise are undeniably good for your heart and vascular system—and some, like swimming and cycling, have been found to reduce cholesterol—more research is needed to determine which are the best at shifting cholesterol scores.

Some of Sperling's research has also examined the benefits of intermittent fasting on cholesterol levels. Intermittent fasting plans come in a lot of different forms, but one type (known as time-restricted eating) has generated a lot of promising research findings. Time-restricted feeding involves a daily fast, usually for 12 to 16 hours, while the rest of the day is open for normal eating. For example, you might eat lunch, dinner, and snacks between the hours of noon and 8 p.m. But the rest of the day, you avoid all caloric foods and beverages. Time-restricted eating has been linked to significant weight loss—which often improves cholesterol scores—as well as lower LDL and total cholesterol.

There are other ways to improve your cholesterol naturally. But focusing on what and how you eat, as well as your exercise habits, is what matter most.

DON'T WAIT TO START

While the health problems associated with high cholesterol and clogged arteries often don't show up until a person's 50s or 60s, the underlying plaque buildup often begins decades earlier—in some cases, during a person's 20s.

Researchers have found that taking steps to lower your cholesterol earlier in life, before that plaque buildup gains momentum, could lead to three-fold reductions in cardiovascular disease compared to delaying these healthy changes until middle age. "The results of our study suggest that an effective primary prevention strategy may be to place greater emphasis on a healthy diet and regular exercise beginning early in life," wrote the authors of a 2012 study in the *Journal of the American College of Cardiology*.

Sperling agrees, and says you could think of cholesterol health as similar to an investment portfolio: the earlier you start, the greater the eventual profit. "You want to start in your 20s, not your 40s," he says.

Even if it's too late to start early, the most important thing is to start. Cho says that changing diet and lifestyle to lower cholesterol can, for example, help those who have heart disease and are already taking cholesterol-lowering medications to avoid stronger drugs and the side-effects they may cause, such as joint pain and muscle spasms. "If you can make changes that prevent you from having to increase your dose, that's a good thing," she says.

Cholesterol problems are one of the most common age-related risk factors for heart disease. While drugs can help, improving your eating and exercise habits can save your heart and vascular system from potentially life-threatening risks. ☐

A HEALTHY DIET IS THE CORNERSTONE OF MANAGING DIABETES

STOCK YOUR KITCHEN WITH THESE HEALTHY FOODS.

Brown Rice
Eating a fiber-rich diet helps the heart, lowers diabetes risk, and keeps the GI system running smoothly, and this hearty staple is a first-rate source. A tip from New York–based nutrition expert Samantha Cassetty: "Keep frozen brown rice at home, and it will be that much easier to throw together healthy stir-fries with plenty of veggies."

Chia Seeds
Tiny chia seeds are loaded with antioxidants and fiber (5 grams in one tablespoon). You need to soak chia seeds or add them to other foods. An easy way to work them in is to add them to your pancake mix. Chia seeds are a great source of heart-smart omega-3 fatty acids.

Coffee
Coffee drinkers reap tons of benefits, including reduced risk of diabetes. And, perhaps, a longer life: A study of more than 200,000 men found that coffee drinkers were less likely to die prematurely. Coffee has polyphenols—phytochemicals that have a prebiotic-like effect and help fuel the health-supporting bacteria in your microbiome, says Cassetty.

Collard Greens
Collard greens are a cruciferous vegetable, which means they help protect against inflammation and even some forms of cancer. As with all fiber-rich vegetables, collards have the power to help ward off type 2 diabetes. They're also packed with nutrients, including the antioxidant vitamins A and C.

Dates
Snack on chewy dates, and you get a whole lot of free-radical-fighting antioxidants (phenolic acid, flavonoids, carotenoids). Some studies suggest that dates qualify as an anticancer and antidiabetic food. They're also full of fiber. One way to enjoy them is by removing the pit and filling the date with almond or peanut butter.

Extra-Virgin Olive Oil
Extra-virgin olive oil (EVOO) deserves its cult status as a long-life food. EVOO is full of anti-inflammatory antioxidants and may lower the risk of cancer, diabetes, heart disease, stroke, and Alzheimer's disease. Use it to sauté your favorite veggies and in place of butter when making omelets.

Greek Yogurt
Greek yogurt—yogurt with the whey removed—is a probiotic, full of healthy bacteria. A strong microbiome with a beneficial mix of bacteria helps your body maintain overall health. In 2024, the Food and Drug Administration announced it will allow yogurt makers to say their products may prevent type 2 diabetes, though the evidence is still mixed.

Green Peas
Peas may look tiny on your plate, but they pack a mighty wallop. Just half a cup provides 4 grams of protein. They're also a low-glycemic-index food, helping to keep blood-sugar levels healthy. Snack on raw or blanched sugar snap peas dipped in hummus or fresh tomato salsa.

Kidney Beans
Kidney beans—along with lentils, chickpeas, black beans, and dried peas—are members of the pulse family. "A higher intake of pulses is linked to a lower risk of type 2 diabetes, heart disease, certain cancers, and obesity," says Cynthia Sass, a performance nutritionist based in Los Angeles and New York City. Replace meat with beans—an excellent plant-based source of protein—in chili, tacos, and soups.

One serving of kidney beans packs 9 grams of protein.

Oatmeal
Research links whole grains in general and this breakfast favorite in particular to a reduced risk of type 2 diabetes and heart disease. In one large Danish study, men and women with the highest intake of oats and rye had roughly a 25 percent lower heart-attack risk than people with the lowest intake.

Parmesan Cheese
Parmesan and other fermented cheeses supply both probiotics and prebiotics. Prebiotics feed your good bacteria, and probiotics are healthy live bacteria that bolster the health of our microbiome. To get the optimal gut benefits, buy the good stuff (Parmigiano-Reggiano) and shave it into salads and over asparagus and other vegetables. Parmesan is lactose-free, and 1 ounce delivers 30 percent of the recommended daily amount of calcium.

Plums
Eaten fresh, plums are packed with anti-inflammatory polyphenol antioxidants, which are linked to many benefits, from reduced risk of diabetes and cancer to heart health. Dried plums (prunes) are famous for taking care of a health annoyance: constipation.

Popcorn
Air-popped popcorn has very few calories, 3 to 4 grams of fiber per serving, and has cancer-fighting potential, thanks to its antioxidant content. One study found that it contains more antioxidant polyphenols than apples and pears. Enjoy your popped corn straight up with sea salt or spritzed with a little oil and dusted with Parmesan and fresh herbs.

Strawberries
Strawberries and raspberries are the best berry sources of ellagic acid, a type of polyphenol that in preliminary test-tube studies prevented skin, bladder, lung, esophagus, and breast cancers. All berries deliver polyphenols, antioxidant vitamin C, and heart-healthy, diabetes-fighting fiber.

THE TRUTH ABOUT INTERMITTENT FASTING AND TYPE 2 DIABETES

SOME WORK ON PEOPLE WITH DIABETES HAS FOUND THAT INTERMITTENT FASTING MAY INCREASE INSULIN SENSITIVITY AND ALSO REDUCE INSULIN LEVELS IN THE BLOOD. THIS IS A BIG DEAL.

BY MARKHAM HEID

MOST FAD DIETS DON'T LIVE UP TO THE hype, let alone serious scientific scrutiny. But intermittent fasting seems to be an exception. These plans involve going without caloric food or drink for an extended period of time—anywhere from 16 hours to several days—and they have become increasingly popular. Research has also found them to be effective for weight loss.

Doctors often advise people with type 2 diabetes to lose weight, which can have beneficial effects on blood glucose and insulin sensitivity, as well as on the progression of the disease. For this and other reasons, experts are actively looking at the effects of intermittent fasting among people with type 2 diabetes—though they caution there are risks associated with the regimen, and that it isn't right for everyone.

"People with diabetes should be those who benefit most from intermittent fasting," says Benjamin Horne, director of cardiovascular and genetic epidemiology at Intermountain Healthcare in Utah. "But these diets also present some of the greatest potential safety issues, because of the medications that people with diabetes are typically taking."

Horne has coauthored several recent papers on the effects of intermittent fasting among people with diabetes. One of them, which appeared in the *Journal of the American Medical Association* in 2020, looked specifically at the risk profile of these practices. "It's so easy to start an intermittent fasting regimen on your own, so our main focus was on the safety issues surrounding fasting when you have a diabetes treatment plan already in place," he says.

For most people with type 2 diabetes—particularly those who are not taking medications to control their blood sugar—the research indicates that intermittent fasting is both safe and likely to be beneficial, Horne says. Here, he and other experts explain the possible risks of intermittent fasting plans, as well as the benefits and best approaches.

THE RISKS OF INTERMITTENT FASTING

Low blood sugar, or hypoglycemia, can cause a rapid heart rate, sweating, shakiness, and other symptoms. If severe, it can induce weakness, seizures, or even death. People with type 2 diabetes are at increased risk for hypoglycemia—especially if they go long periods without eating—and this was one of the first dangers experts looked at when assessing the safety of intermittent fasting. "If you are taking medications that are aimed at reducing the amount of glucose in your blood together with fasting, these can cause potentially fatal hypoglycemia," Horne says. "It's not a minor safety risk."

For a 2018 study in the journal *Diabetic Medicine*, researchers in New Zealand found that the incidence of hypoglycemia did increase among people with type 2 diabetes who attempted intermittent fasting. However, this increase was in line with the results of other weight-loss diets, including conventional approaches that encourage people to consume fewer calories on a daily basis. Also, the people in the study were all taking drugs designed to reduce blood glucose. "It was the medications, rather than the diet per se, that caused the hypoglycemia," says study author Brian Corley, a diabetes specialist at Capital & Coast District Health Board, in New

Zealand. Corley says that people who are taking these drugs could reduce their risks for dangerous drops in blood sugar by working closely with a physician, monitoring blood sugar more carefully on fast days, and educating themselves on how to manage a hypoglycemia episode. In other words, intermittent fasting plans aren't necessarily off the table for these patients; they just require a little more care. Meanwhile, his study also found that intermittent fasting aided weight loss and improved measures of fasting blood sugar, hemoglobin A1C, and overall quality of life.

For people who aren't taking drugs to lower their blood sugar, Horne says the risk of hypoglycemia seems to be very low. "People should still consult with someone who treats diabetes—a physician such as an endocrinologist or at least a nutritionist who is trained in diabetes treatment," he says. Like Corley, he says even people on blood-sugar medications could attempt intermittent fasting, so long as they are working with an expert. "It's not so much should they or shouldn't they. It's more the degree to which they should be monitored," he says. (This does not extend to patients with type 1 diabetes; Horne says that for that group, intermittent fasting is too risky.)

Aside from hypoglycemia, a second major concern is dehydration. High blood glucose causes general dehydration in the body, and people with type 2 diabetes are already at an elevated risk. Intermittent fasting may further increase these risks if people are drinking or eating less than they normally would. (Food, it turns out, can provide one third or more of the water that a person consumes each day.)

"With dehydration, people with diabetes can have a variety of negative outcomes," Horne says. Stroke, migraine headaches, and kidney damage are potential problems, especially if a person with diabetes has other health conditions related to these risks. "So if someone already has a problem with their kidneys—and oftentimes people with diabetes have some kind of kidney issue, if not full-blown kidney disease—dehydration can potentially cause harm," he explains. While drinking water or other noncaloric liquids while fasting can reduce these risks, people who have type 2 diabetes along with other chronic diseases—such as heart disease or kidney disease—probably shouldn't attempt fasting diets. The same goes for older, frail people with diabetes. "Fasting puts stress on the body and organs," he says. If you're weak or unwell, going without food is probably a bad idea.

There are a few more potential health concerns associated with intermittent fasting, though they are not specific to people with type 2 diabetes. For example, nutrient deficiencies, inadequate protein intake (especially if you're older), and other forms of malnutrition are possible if you're fasting. Also, the safety profile of intermittent fasting is not well mapped among women who are pregnant or breastfeeding or among young kids—groups with important nutritional requirements different from those of the general population. These groups should not fast until the risks and benefits are better understood, experts say.

While hidden dangers could emerge, intermittent fasting—with expert oversight—seems to be safe for most people with type 2 diabetes.

THE BENEFITS OF INTERMITTENT FASTING

While intermittent fasting may present risks for some, it could also provide benefits over and above other approaches. A 2017 study in the *World Journal of Diabetes* found that just two weeks of intermittent fasting led to significant weight loss (more than 3 pounds, on average) as well as improvements in glucose levels. "It's possible that intermittent fasting could lead to reduced insulin resistance," says Kerry Mansell, coauthor of that study and a professor in the College of Pharmacy and Nutrition at the University of Saskatchewan, in Canada.

Research supports this hypothesis. Some work on people with diabetes has found that intermittent fasting may increase insulin sensitivity and also reduce insulin levels in the blood. This is a big deal. "Essentially, fasting is doing what we prescribe diabetes medications to do, which is to improve insulin sensitivity," Horne says. At least one small trial (of just three people) found that adopting an intermittent fasting diet allowed diabetes patients to stop taking their insulin drugs altogether. That study's findings still need to be replicated in a larger group. However, these sorts of results are encouraging. Insulin resistance is associated with higher levels of inflammation and other risk factors for cardiovascular disease. "Even when people aren't losing weight on a fasting regimen, some research has found that insulin sensitivity improves markedly," Horne says. "This is something you typically don't see with other caloric-restriction diets."

How could fasting be producing these benefits? There are a handful of theories, and more research is needed, but several hypotheses may turn out to be true. One leading one—which is supported by solid research—is that fasting kicks off a kind of cellular cleansing process that removes old or unhealthy cells and allows new ones to flourish. Based on this work, some experts argue that the human body isn't designed for the modern food environment and its three-meals-a-day-plus-snacks eating schedule. They say intermittent fasting may more closely resemble the way humans ate for most of our species' history.

WHICH FASTING PLAN IS BEST?

The term intermittent fasting does not refer to a single well-defined practice. Several different approaches fall under the intermittent fasting umbrella. The three most common and well-studied are known as time-restricted eating, alternate-day fasting, and the 5:2 diet.

The first of these—time-restricted eating—involves consuming your day's calories during a single "feeding window" of six to eight hours. For example, someone on this diet may eat between noon and 6 p.m. each day and avoid all caloric foods and drinks for the other 18 hours of the day. Meanwhile, someone on an alternate-day-fasting diet eats normally one day, but the next day consumes few or no calories. Finally, the 5:2 diet involves eating normally five days a week but fasting on the other two days.

There are many variations of each of these plans. At this point, it's unclear which of these, if any, is optimal for people with type 2 diabetes. "I think time-restricted eating is probably the most common, followed by fasting two days a week," Horne says. "But at the moment, I would say there is not one plan that stands out as a best option." The "right" plan, he adds, is the one a patient will stick with. Even if the more intense fasting programs turn out to be the most beneficial, that doesn't really matter if a person can't adhere to one.

HOW TO START INTERMITTENT FASTING

The first step, always, is talking with your physician or care team. They should be able to help you weigh the benefits and risks, identify dietary approaches to avoid nutritional deficiencies, and, if necessary, adjust medications you're taking to avoid problems. "Safety must come first," Horne says.

Don't be surprised if your health care provider isn't enthusiastic about fasting diets, given that there are risks associated. These plans are still relatively new, and they're generally not taught in medical school. "People may encounter pushback, or their physician may not be very familiar with these regimens," Horne says. If your doctor says that fasting isn't right for you, that's one thing. But if she or he seems dismissive of fasting diets in general, it may be worth seeking a second opinion from a provider who has experience with these plans, as there is evidence that intermittent fasting may be a helpful or even superior alternative to classic weight-loss plans for people with type 2 diabetes. □

MANAGING YOUR BLOOD SUGAR

BE CONSCIENTIOUS. ESTABLISH A ROUTINE. TRY A CONTINUOUS GLUCOSE MONITOR. PEOPLE WITH TYPE 2 DIABETES OFFER TIPS ON WHAT'S WORKED FOR THEM.

BY ELIZABETH MILLARD

IF ONLY THERE EXISTED A SIMPLE SET of rules for managing blood sugar when you have type 2 diabetes—it would be one of the most requested pamphlets in a doctor's office. Instead, as many people find, there's no one-size-fits-all solution beyond trial and error and time and effort to discover what works best.

One way to speed up the discovery? Learn from others who are living with the condition. Here, seven people with diabetes share their insights and experience.

PAY CLOSE ATTENTION TO FOOD AND 'MEDICATION EFFECTS'

When Agnes Czuchlewski, 70, was diagnosed with type 2 diabetes more than 20 years ago, her first thought was that she had to implement iron-clad restrictions on her eating and would never have a sugary treat again. That didn't last long. "You can become obsessed with what you 'should' be doing, but that's exhausting," she says. "Instead, it's much better to educate yourself about how your choices affect you. For example, have that candy bar, but look at what happens to your blood sugar—how much it goes up and how quickly—when you do. Then you can implement controls based on what you need."

Paying attention to how medication affects you is also important. Czuchlewski's initial medication lowered her blood sugar so dramatically that she became hypoglycemic at night, a dangerous situation in which blood sugar drops too low. At one point, she feared she wouldn't wake up. Tracking the effect over several nights provided her with the data

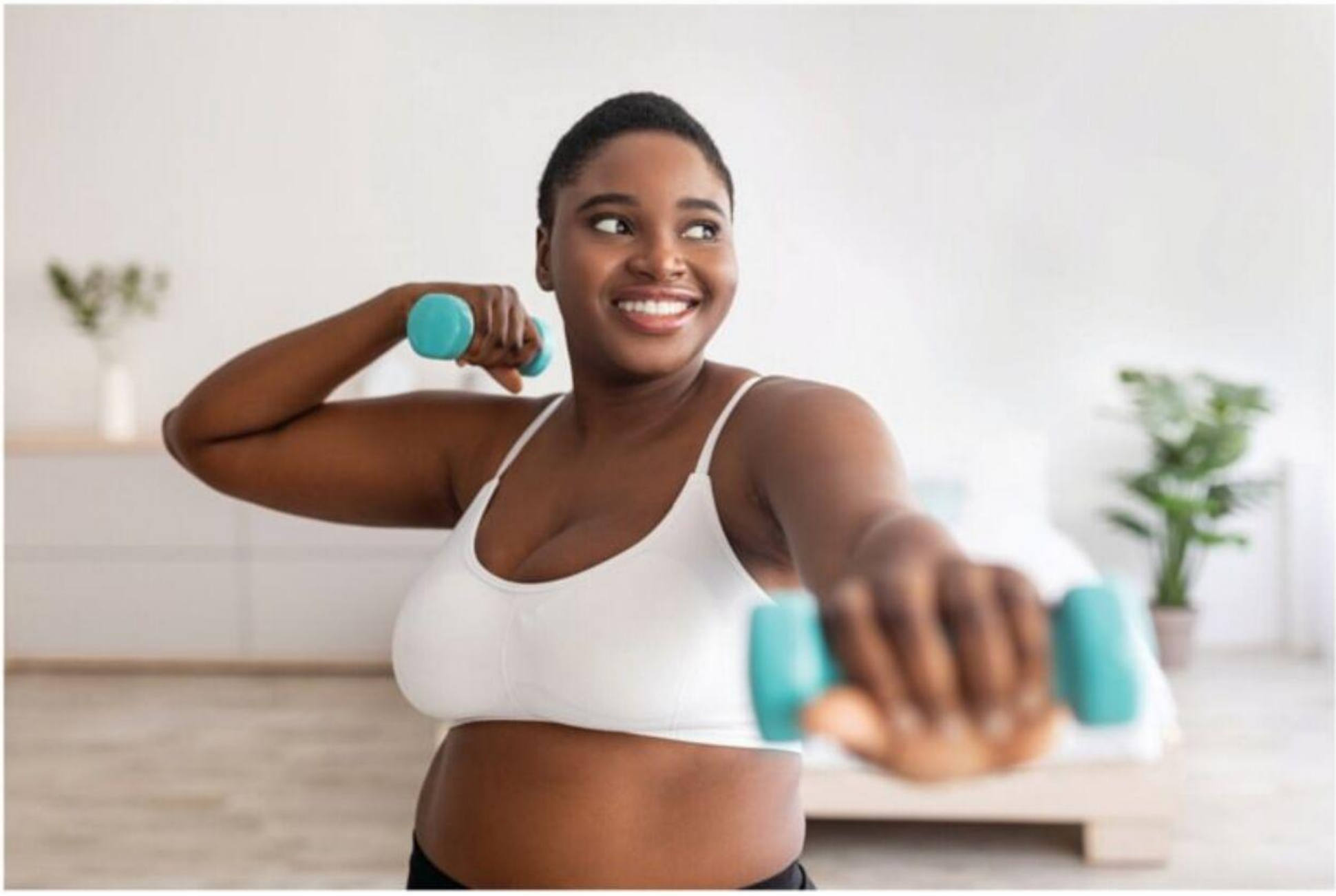
she needed for another conversation with her doctor, and for a medication switch.

"Learn about your body, and be more aware of how medication is affecting your numbers, how each food choice is affecting you," she says. "When I was diagnosed, four other people in my work group were diagnosed within six months of each other. Each one of us reacts to their meds and to different foods in unique ways. Don't assume you'll react a certain way just because someone else with diabetes does."

Without truly observing how your body responds to each medication—a sudden wave of fatigue, for instance, or symptoms like increased thirst or weakness—it's difficult to understand the subtle and overt ways that blood sugar may be affecting you overall. Taking time to slow down and build body awareness can go a long way toward managing blood sugar more effectively.

CONSIDER A CONTINUOUS GLUCOSE MONITOR

Tim Jones, 58, has lived with type 1 diabetes for 37 years, and the greatest lesson he's learned is that blood-sugar regulation can change over time and how much insulin he needs can vary accordingly. He



needs to not only monitor his carbohydrate and fat intake—both of which affect insulin production—he needs to stay on top of his exercise regimen, and mix things up.

One game changer for Jones was switching from an insulin pump to a hybrid closed-loop artificial pancreas system with a continuous glucose monitor (CGM)—a small, wearable device that tracks blood-sugar levels throughout the day. The technology, now used widely, was novel at the time and allowed him to worry less about his levels dropping too low. He still had to keep diabetes in his mind constantly—the pressure is "relentless" he says—but it was nice to have a little something in his pocket to share the load, especially when he was sleeping. It was a relief, he adds. "I have never been in better control than I am right now," Jones says, "and I'm expecting technology to get better."

Using a CGM may be particularly useful for those who have found traditional manual methods of monitoring blood sugar to be challenging. For example, Max Androsiuk, 36, tried managing his blood sugar for five years after his type 1 diabetes diagnosis but found it so difficult that he had to quit playing basketball with his friends, in part because he would get nervous about the activity, and that anxiety increased his blood sugar. Once he started wearing a CGM, he could quickly glance at an app on his smartphone and know what to do and get back on the court. "I can easily control my blood sugar by applying measures I know will work if I see my numbers go up or down," he says.

A high glucose reading does not mean having to stop exercising. Instead, try relying on methods you know work to help bring your numbers under control.

ESTABLISH A ROUTINE

Constantly monitoring your diet, sleep schedule, stress levels, exercise routine, and medication can not only feel like a juggling act, it can be overwhelming, says Emilee Herringshaw, 30. Just getting a high reading might send her into a tailspin: Should she go for a walk or a run? Drink some water? Contact her doctor?

Having a regular routine helps steady her when there are fluctuations in her blood sugar. "My daily regimen is reliable yet modifiable," Herringshaw says. It involves reviewing her blood sugar at specific times, being mindful of when she takes her medications, focusing on stress-management practices, and preparing food in advance so she knows the carbs, protein, and fat content in each meal. The routine has helped her identify trends that made her feel out of control. "Getting into a regular pattern of tracking, exercise, and preparation makes me feel physically and mentally better." she says.

KEEP A CONSISTENT EXERCISE SCHEDULE

There are many upsides to exercise for people with diabetes. Depending on how long you're active and the intensity of your workout, being active can lower blood sugar for 24 hours or more, according to the American Diabetes Association. Physical activity also makes the body more sensitive to insulin, and both help control blood sugar and lower the risk of heart disease and related nerve damage.

For Jenny Lyn Belleza, exercise has been the cornerstone to managing her type 2 diabetes. "I try to stay on top of my fitness by going to the gym a few times a week and doing some sort of cardio or strength training," says Belleza, 37. "I've found this helps keep my blood sugar in check and prevents any spikes or dips throughout the day."

While creating an exercise program, check in with your doctor or diabetes educator to make sure you consider all the right factors. If you're taking insulin, for example, you may need to adjust the dose before exercise to lower your risk of hypoglycemia. Much like tracking how food affects your blood sugar hour by hour, keep on top of blood-sugar changes before, during, and after activity to understand how working out is affecting you.

WORK WITH A CARE TEAM

Melissa Almeida was just a teenager when she was diagnosed with type 2 diabetes, and for years she struggled with nearly every aspect of managing the disease, from medication timing to food choices. "I felt overwhelmed, and as a result, I was only taking one of three prescribed medications," says Almeida, now 50. "I wasn't able to maintain a steady level of energy and it affected every aspect of my life, including being able to work."

Almeida was a full-time working mother by the time she contacted UMass Memorial Health about diabetes coaching. The program provided her with counseling on the medications she was taking in order to learn how they affected her blood sugar and what side effects could occur. She also received detailed nutrition guidance that made a big difference for her blood sugar and energy levels. "I felt like I was part of my own care team, helping to ensure my care plan and individual goals were being met," Almeida says.

The strategy is backed up by plenty of research, including a 2019 study of customized diabetes-education programs that appeared in the *International Journal of Environmental Research and Public Health*. In it, researchers found that participants, who used CGMs to track their results, saw significant improvement in how they managed their type 2 diabetes in just three months.

KEEP MENTAL HEALTH IN MIND

After 25 years as an endocrinology patient at Geisinger Health in Pennsylvania, Shivaun O'Donnell, 64, decided to get more involved with care for other patients and became a diabetes educator. It's been a decade now, and along the way she's learned a wide array of strategies for blood-sugar management. One she's found personally meaningful is focusing on emotional well-being. "This condition can come with depression and, honestly, life-stopping anxiety," she says.

> **"A LARGE PART OF DIABETES MANAGEMENT IS MENTAL. YOU CAN DO EVERYTHING RIGHT, BUT IF YOU'RE FEELING ANXIOUS OR DEFEATED, THAT MIGHT END UP SABATOGING YOUR EFFORTS," SAYS A PATIENT.**

In fact, insulin resistance can double the risk for major depression and cause symptoms like fatigue, sleep disturbance, and loss of appetite—all of which can impact blood-sugar regulation, according to research from Stanford Medicine published in 2021. As few as a quarter of people with diabetes who have depression get diagnosed, according to the CDC.

"A large part of diabetes management is mental," says O'Donnell. "You can do everything right, but if you're feeling anxious or defeated, that might end up sabotaging your efforts." That's why it's important to focus on tactics that will boost your brain as well as your body, and to pursue activities that are fun for you. "This isn't just about your blood sugar," O'Donnell says. "It's about learning to love your life." ◻

BARIATRIC SURGERY DELIVERS RESULTS

THE PROCEDURE IS CONSIDERED THE GOLD STANDARD IN TREATING THE DISEASE, YET ONLY A TINY FRACTION OF ELIGIBLE PATIENTS SIGN UP.

BY MARKHAM HEID

THE TERM BARIATRIC IS DERIVED FROM the Greek words for "weight" and "to treat." Originally, as the name denotes, this form of surgery was aimed at helping people manage obesity. But as medical science's understanding of bariatric surgery has improved, experts have recognized that these procedures could also help people with obesity-related health conditions, including type 2 diabetes.

"In 1999 when I was a junior resident in general surgery, I was struck by the observation that patients who had this type of surgery were very rapidly seeing improvement in their diabetes," says Dr. Francesco Rubino, a pioneer in research on the antidiabetic effect of certain bariatric procedures and now chair of metabolic and bariatric surgery at King's College London. "Even patients who had very severe diabetes would get to normal levels of blood sugars and could stop taking medication," he adds. "It always seemed to me like the magnitude of improvement was too much just to be the by-product of weight loss."

Rubino wasn't the only one noticing these effects. One early study from researchers at East Carolina University, for example, found that 83 percent of patients with type 2 diabetes who underwent gastric bypass surgery experienced long-term remission of the disease. Yet because improvements in the disease were attributed exclusively to reductions in body weight, surgery at that time was not considered a primary treatment option.

Flash forward to today. Experts continue to debate precisely how bariatric procedures benefit people with type 2 diabetes, but research has established that the procedures are effective. One long-term trial, published in the *New England Journal of Medicine*, found that adding bariatric surgery to nonsurgical diabetes care led to major improvements in patient outcomes. People in the study who underwent surgery were more than three times as likely to achieve normal blood-sugar scores one year after treatment. They were also less likely to be on glucose-lowering medications, and they reported greater quality-of-life improvements.

"Surgery can actually put diabetes into remission, and it's safe and cost-effective compared to standard nonsurgical care," says Dr. Carel Le Roux, a professor at University College Dublin who studies bariatric surgery for people with diabetes. "It's currently the best treatment we have for type 2 diabetes, and I'm an internal medicine doctor, not a surgeon, so I have no vested interest in talking up surgery."

It seems the message has not reached the public, since only 1 percent to 2 percent of patients eligible for the bariatric procedures get them, according to Dr. Andrew Kraftson, a clinical associate professor and director of the post-bariatric program at the University of Michigan. And while surgery is not what Le Roux refers to as "a silver bullet"—and not everyone with type 2 diabetes is a candidate—many more people should consider it, both physicians agree.

Here, experts discuss the benefits and risks of bariatric surgery for type 2 diabetes, the procedures themselves, and how combining surgery with medication may ultimately provide the best long-term results.

HOW DOES BARIATRIC SURGERY BENEFIT PEOPLE WITH DIABETES?

It's the million-dollar question, and it has more than one correct answer. Le Roux's view is that weight loss is the dominant mechanism, but that in addition there are other mechanisms at play. Type 2 diabetes is a disease of too little insulin and too much blood sugar. Excess body weight increases the amount of insulin needed to manage the blood's sugar levels, and so it exacerbates the imbalances that give rise to diabetes. There's also evidence that adipose (fat) cells release by-products that may damage the pancreas, which is where insulin is produced. These are just some of the reasons why losing weight is associated with improvements in diabetes.

Something else—something beyond these weight-loss benefits—is clearly going on. "We see some individuals who are on hundreds of units of insulin leave the hospital following surgery requiring no insulin, and that predates weight loss," says Kraftson. "This is a bit of a controversial area, but some data suggest that there are unique properties to the surgery itself that produce metabolic benefits."

The most common bariatric procedures for people with type 2 diabetes are Roux-en-Y gastric bypass surgery and sleeve gastrectomy. Both procedures involve shrinking the size of the stomach, either by removing a portion of it (sleeve gastrectomy) or dividing it into two sections and connecting the smaller of the two portions to the small intestine (gastric bypass).

"It's clear that the stomach and the intestine are not just a digestive organ, but also an endocrine organ," says Rubino, adding that "the gastrointestinal tract produces a huge number of hormones, and all of them are involved in sugar metabolism and insulin production." What's more, bariatric surgeries affect the stomach and gut's populations of microbes, which themselves produce metabolites that play a role in sugar metabolism. "These are just a few of the mechanisms that may explain why operating on the gut can exert such a huge influence on diabetes even absent weight loss," says Rubino.

In fact, Rubino and other health care professionals who treat people with diabetes have begun referring to bariatric surgery as "metabolic surgery," in order to emphasize that it's not just about reducing body weight.

WHO SHOULD CONSIDER BARIATRIC SURGERY?

Right now, the criteria are fairly straightforward. The National Institutes of Health guidelines say that anyone with type 2 diabetes and a body mass index (BMI) of 35 or higher is a candidate. If your BMI is between 30 and 35 and your diabetes isn't responding well enough to medications and lifestyle changes, surgery may also make sense. Le Roux echoes Kraftson's sentiments, saying that anyone with type 2 diabetes who has been on medications and hasn't gotten their blood sugar under control should be considered for surgery, regardless of BMI. "I think surgery should be on the table and being discussed for a lot more patients," he adds.

There are a number of hurdles at play. One is that in the lower-BMI group, insurance may not pay for the procedure. What's more, obesity is a stigmatized disease, Kraftson says, and some people may have an aversion to undergoing a surgical procedure that traditionally is performed only on those with severe obesity. "Also, people focus on the one person they know who had [the surgery] and regained all the weight," he says.

Though not the experience of most patients, it can happen. "The potency of the surgery does wane over time, and some people do regain weight or have a reactivation of their diabetes," says Kraftson. One 2020 study found that, three to six years following a sleeve gastrectomy or Roux-en-Y gastric bypass procedure, about one quarter of patients had regained their weight. "A majority of people only need surgery and then the job is done," says Le Roux. "But there's a subset of people who either don't have a good response or they have a relapse later." Among people who have the procedure at a younger age—something that is increasingly common, as type 2 diabetes rates increase in people under 40—weight regain or diabetes relapse may be more likely.

The surgery comes with additional risks and costs. "Approximately 1 in 20 people will have a significant complication," Le Roux says. Those include gastrointestinal bleeding, infections, or leakage. Embolisms or thromboses, which can be life-threatening, are also possible. "All these tend to happen early on, which is why we keep people in the hospital for one or two nights," he says.

Finally, metabolic surgery requires major lifestyle adjustments. Following the surgery, people must adopt a specialized diet and exercise regimen to maintain health and facilitate weight loss. Eating

For the subset of people who undergo surgery and don't have a good response or who relapse, some newer medications may prove helpful.

too much or too quickly can cause symptoms such as gut cramps, pain, and diarrhea. Also, things a person once loved to eat—even healthy foods—may not taste the same or provide the same pleasure. Alcohol is initially off limits. Even after full recovery, people have to be very careful with how they drink. Finally, to avoid nutrient deficiencies, it's necessary to take several daily supplements. "You normally have to take a multivitamin twice a day, and calcium three times a day, so it's a lot of work to prevent these deficiencies," Kraftson says.

Even in people who do everything right, surgery is not always successful. Understanding why some people don't respond well—and figuring out how to prevent a poor response—is "the cutting edge" of today's research on surgery for type 2 diabetes, according to Le Roux.

THE FUTURE: A MIX OF SURGERY AND MEDICATIONS?

One of the big stories in both obesity and diabetes care is the arrival of new injectable drug medications that, at least in clinical trials, have been shown to help people with obesity lose significant weight—in some cases 20 percent or more. "Lots of people think these drugs will be the death of bariatric surgery," Le Roux says. "I don't agree, and I think a large number of patients will have surgery plus medications, but at a lower dose."

The majority of people who undergo surgery—roughly 70 percent of patients, he says—experience sustained weight loss and diabetes remission without the aid of drugs. But for the subset of people who either don't have a good response or who eventually relapse, some of these new medications may prove helpful. "The answer may not be surgery instead of medicine, but medicine with surgery," he says.

Others share his view. "We find that some of these weight-control medications work synergistically with surgery, so they enhance portion control and satiety," Kraftson says. It's yet to be seen whether the newest drugs enhance patient outcomes when combined with metabolic surgery. But this is a distinct possibility and could become the standard of care for people with both obesity and hard-to-control diabetes.

Rubino says the big message for people with type 2 diabetes is that surgery may provide the best hope for lasting remission. "We're taught that type 2 diabetes is a chronic, progressive, irreversible disease," he says. "But full remission is possible with surgery, and it's possible in a majority of patients." □

CHAPTER 4

THE ROAD AHEAD

NEW TECHNOLOGIES AND MORE EFFECTIVE MEDICATIONS ARE CHANGING THE NARRATIVE AROUND DIABETES.

PROJECT OPEN INSULIN

IN 2019, *TIME* VISITED A GROUP OF BIOHACKERS HOPING TO REVERSE ENGINEER THE WAY THE DRUG IS PRODUCED AND TURN OVER THE INSTRUCTIONS TO THE PUBLIC.

BY GRANT BURNINGHAM

IN A HIP OAKLAND, CALIFORNIA, neighborhood, just blocks from cocktail bars and swanky Mexican restaurants, is an enormous warehouse, home to Counter Culture Labs, ground zero for an audacious challenge to the high cost of prescription drugs. In the entryway stands a one-and-half-story-tall cardboard T. Rex, and inside, it's as if Dr. Frankenstein were sharing his lab with a hoarder: Cluttered shelves hold piles of drying mushrooms, Clorox wipes, wires, kitchen pots, motor oil, two books about Darwin, ropes, a broken alarm clock, a telescoping magnifying glass, a heat gun, a 3-D printer, and several jars of clear liquid with tubes running between them. One shelf holds plastic bins labeled LAB COATS, PAINT & BRUSHES, and EBOLA SUITS.

A group of professional scientists and amateur tinkerers founded Counter Culture Labs in 2013 with the goal of bringing biotechnology to the masses. At any time, it hosts dozens of projects; when I visit, there's one whose objective is to make "vegan cheese" using yeast.

The Open Insulin Project has bigger plans. The group wants to reverse engineer how the world's largest pharmaceutical companies produce insulin and then turn over the instructions to the public. In theory, anyone with a bit of cash could then build a DIY lab in their garage and make open-source insulin.

Currently three companies—Eli Lilly, Novo Nordisk, and Sanofi—control most of the world's $27 billion insulin market, using a complicated web of regulations and patents to keep a hold on it. Open Insulin wants to rebuild it with no megacorporations and no profit. The project is probably months, if not years, away from actually making medical-grade insulin, but its objective is as much political as it is production-oriented: bringing a sharp focus to the stratospheric price of insulin and, more broadly, the predatory pricing of prescription drugs in the United States.

Over the past 60 years, the list price of a vial of insulin has gone from about 75¢ to $250—an increase nearly 43 times the rate of U.S. Consumer Price Index inflation. "High drug costs exist throughout

The global insulin market is dominated by Eli Lilly, Novo Nordisk, and Sanofi.

the system, but insulin is the poster child of this broken marketplace," says Representative Tom Reed (R., New York), one of the chairs of the Congressional Diabetes Caucus. Some, in fact, think that the project is already working as a kind of provocation: a way to force the issue on what is really a policy problem. "If the price of insulin gets regulated, the project will just go away," says Jean Peccoud, a professor of chemical and biological engineering at Colorado State University.

For now, the project seems to be in a regulatory safe space, but that may change as it gets closer to making actual medicine. In an email, a Food and Drug Administration (FDA) spokesperson acknowledged that the agency is aware of the Open Insulin Project, but noted, "We cannot comment on hypothetical situations or potential future states of regulation."

Predatory pricing in the U.S. isn't unique to insulin. A study of the world's top 20 medications found that Americans pay an average of three times as much as patients in the U.K. do for a given drug. The science behind making insulin is old, which makes it a good first target for the disruption of the pharmaceutical industry.

Anthony Di Franco, one of the Open Insulin Project's cofounders, has diabetes himself, and has watched as the price of managing his disease has gone up and up. He has a dual undergraduate degree in physics and math/computer science from Yale University and is currently on leave from pursuing his Ph.D. in computer science at the University of California, Davis. He lives on contracting jobs, doing data science, and researching machine learning and programming languages. Like many freelancers, he doesn't have employer-sponsored insurance. But unlike most with the disease, he knew enough about science to start thinking there might be a better way. In 2015 he launched the Open Insulin Project."The current system was built to exploit people with diseases," Di Franco says. "Historians will look back and say, 'How could they have done such a terrible job?'"

Diabetes is caused when the pancreas can no longer make enough or any insulin, a hormone that regulates blood sugar, or when a person's body builds up a resistance to the hormone. Insulin, which helps the body use sugar for energy and lowers sugar levels in the blood, was first used to treat diabetes in the early 1920s. Physician Frederick Banting and

Anthony Di Franco, founder of the Open Insulin Project, at a lab in Oakland.

medical student Charles Best were working with dogs, inducing diabetes by removing their pancreases and then trying to figure out a cure. The two eventually extracted a substance from cow pancreases; purified it with the help of biochemist James Collip; and proved it worked by injecting it themselves and noting that they got dizzy, a sign of low blood sugar. By 1922, doctors were using insulin from cow pancreases to treat diabetes patients.

People with severe diabetes need insulin injections to stay alive. Without it, your blood turns acidic, your body dehydrates, your vision blurs, you get weaker and start to vomit. Over days, you slowly—and painfully—die.

This fact, coupled with the inefficiencies of the American health system, as well as a manipulable patent framework, has enabled pharmaceutical companies to steadily increase the price of the lifesaving drug, even as it's become easier and less costly to produce. Generally speaking, drugs are cheap to make. The costs are mostly to pay for the research and development required to discover them. For example, one 2016 study that looked at 106 recently approved drugs from 10 different companies found that the average R&D cost for each was $2.78 billion, compared with only about $19 million per drug in costs of actual clinical trials.

Much of the industrialized world has some form of single-payer health insurance and strict price controls on drugs, usually determined by a board of doctors and experts. In the U.S., the pull of the free market was supposed to keep prices down but instead has led to a complex system of profit-driven corporations, from manufacturers to insurance companies, who add cost at every juncture.

It wasn't meant to be this way, especially not with insulin. Banting, who shared a 1923 Nobel Prize for his work on insulin, demanded his name not be put on the patent, believing that profiting from a medicine was unethical. His codiscoverers agreed, transferring their patents to the University of Toronto for $1 each.

The pharmaceutical corporation Eli Lilly and Company, of Indianapolis, offered to help the university develop the medication, and the school eventually agreed to license the technology. Lilly contracted with slaughterhouses to receive pig pancreases by railroad car, in order to squeeze out the insulin. It was crude, but effective—and cheap. Ads from the 1960s show vials of insulin available for

84¢ in the U.S., just $7.36 in today's dollars. And then came a real breakthrough.

In 1982, Lilly introduced insulin made by genetically modified *E. coli* bacteria. The new insulin was less likely to cause allergies than the animal version, and it could be grown in vats. Novo Nordisk started making its own bioengineered insulin in 1991, and it looked like the drug was about to get really affordable, thanks to the competitive marketplace. Instead, prices went up. A congressional report written in 2018 found that the list price of competing insulin formulations "appeared to rise in tandem," doubling from 2012 to 2018. According to the report, that was most likely due to limited market competition and to the fact that "each part of the insulin delivery chain is controlled by a small number of entities." The marketplace never became competitive.

In theory, the U.S. patent system, which gives manufacturers sole rights to a drug formulation for 20 years, should eventually enable other drug producers to bring cheaper versions of the same medication to the market. But as Reed and the cochair of the Congressional Diabetes Caucus, Diana DeGette (D., Colorado), note, companies skirt this by "evergreening" their drugs—tweaking drug formulas slightly, often making incremental improvements, to renew the patent and prevent generics from ever entering the market. Lantus, a long-acting insulin patented by Sanofi in 1994, was due to enter the public domain in 2015, but instead the company filed 74 patents for newer versions of the drug, which delayed that until 2031. Novo Nordisk has done something similar with one type of insulin by upgrading the mechanics of its injection pen. These insulins are touted as improvements, although there is evidence these are typically minimal.

"People with diabetes experience different issues and complexities that can't be covered by one solution, which is why we continue to bring forth programs that will directly benefit even more patients and work toward much needed longer-term systemic reform," said a Novo Nordisk spokesperson in an email.

An Eli Lilly spokesperson told TIME in an email that the company does not evergreen. "None of our insulins is patent-protected and our most commonly used insulin, Humalog 100, lost patent protection in 2014," the spokesperson said. While the patent for Humalog 100 has expired, because of the complexities of entering the market, only one manufacturer jumped in to make a version of the drug: Sanofi, which already makes its own formulation. Sanofi's "generic" version of Humalog sells for just 15 percent less than its original price. Eli Lilly is also manufacturing an "authorized generic" version, currently selling for 50 percent of the price.

A Sanofi spokesperson, meanwhile, writes that the company's original patent on Lantus has expired and subsequent patents "are related to new and unique inventions." They also point out that despite increases in the listed price for Lantus, the actual price customers pay is lower than it was in 2006, a result of other inefficiencies in the market. The spokesperson added that "we also support a robust and competitive marketplace, including efforts by other organizations to develop new technologies and medicines—including Open Insulin Project."

For insured diabetics, the high costs of insulin are borne primarily by their insurers and so remain more or less hidden. But for those without insurance or for people on high-deductible plans that require them to pay for their own care until they hit a predetermined amount, these prices take lives. Alec Smith, a 26-year-old restaurant manager, couldn't afford the $1,300 a month it took to manage his diabetes. In 2018, Smith was three days from a paycheck when he died alone in his apartment; investigators later found an empty insulin-injection pen in Smith's home. The case made headlines, but the human price of the high cost of insulin isn't hard to find. Some 13.2 percent of the 2.9 million people who take insulin in the U.S. do not take it as prescribed, and 24.4 percent asked their doctor for a lower-cost medication, according to the CDC.

It's not going to take a Nobel Prize to make DIY insulin, just persistence. The good news for the Open Insulin Project is that it has the accomplished 33-year-old French biochemist Yann Huon de Kermadec as its lead scientist. He's in the United States right now because his wife, Louise Lassalle, is a postdoctoral researcher at Berkeley Labs. Huon de Kermadec donates his time, showing up at the lab five to six times a week to work long hours designing a new form of life: a yeast cell genetically engineered to produce a form of insulin people could use.

On his side is the fact that biotech is getting cheap. The same pressures that brought down the cost of total gene sequencing, from a taxpayer-funded $2.7 billion project to a $200 drugstore test, all in

Open Insulin Project head scientist Yann Huon de Kermadec at the Omni Commons Counter Culture Labs, in Oakland.

under two decades, mean you don't need millions of dollars to start a biotech project anymore. The Open Insulin Project is able to do what it does because equipment has become so cheap and powerful—especially in the Bay Area, where high turnover in the biotech industry has lead to a glut of secondhand, lab-quality gear. There are now several companies that market vast databases of genes, searchable by utility, all of which are economical. Huon de Kermadec picked two sequences of genes: one that produces a protein that can be cut to make insulin and one that makes the yeast resistant to a specific antibiotic.

Using these genes, he and the team created a formula for a plasmid, a tiny circular piece of DNA. Then he hired a company to manufacture a small quantity of these plasmids, which they sent to Counter Culture Labs in a tiny plastic vial. Dozens of companies offer this sort of service in the U.S., at prices as low as a few hundred dollars. Next, the team jammed the plasmids into yeast cells, and added an antibiotic solution to the cell cultures. That's where the antibiotic-resistance gene comes in handy—the ones that successfully adopt the plasmid into their own DNA will survive, and those that don't will die out. The next step would be to grow the surviving cells, which should contain the genes to produce both antibiotic resistance and the precursor protein for insulin.

The team thinks they've gotten this far. They

know the yeast produces a molecule the size of insulin—which is a pretty good sign it is, in fact, insulin. But they're scientists, so they're not popping the champagne yet. They want to confirm that the molecule is indeed insulin by using mass spectrometry, a precise technique that allows scientists to identify specific proteins, before they say for sure.

Then they will have to prove their insulin is pure enough to inject into a person. They'll also have to demonstrate they can make medical-grade insulin every time with their process. Then, to get it to the people, they'll need to standardize the equipment so other people can manufacture or buy it.

THE GROUP PLANS TO SHARE ITS INSULIN-PRODUCTION FRAMEWORK ONLINE, WHICH WOULD INVOLVE CROSSING STATE LINES, SO THERE MAY BE OTHER LEGAL ISSUES ON THE HORIZON.

When asked if he thought his team would eventually create a yeast that could produce insulin, Huon de Kermadec responded confidently. "Yes, of course," he says, "it isn't rocket science." But then there are the regulatory hurdles.

Di Franco has been reading up on the history of democracy in ancient Athens and is trying to craft his organization's bylaws in the spirit of the world's first democracy. He also wants its product to be democratically affordable: Di Franco thinks roughly $10,000 should be enough to get a group started with the equipment needed to produce enough insulin for 10,000 people. Each of these $10,000 setups would be somewhere between a middle-school science experiment and an industrial laboratory, and would require rooms of equipment—think something closer to a medical-grade brewery than a countertop bread machine. The resulting product, he says, would cost someone with diabetes dozens of dollars a month instead of hundreds.

That's noble, in theory, but there's a reason why the FDA puts a lot of effort into certifying the labs that make our medicines: mistakes can be fatal. The U.S. drug-development system may be expensive, but it does guarantee quality.

The Open Insulin Project falls into a black hole outside of FDA regulation, according to Peccoud, the Colorado State professor. For one thing, the project may skirt some regulations by being a nonprofit. Also, the FDA allows individuals to largely do whatever they want to themselves. "If you want to inject yourself with home-brew beer, there's no law to stop that," says Peccoud.

If it does reach a production phase, Open Insulin would have to conform to Good Manufacturing Practice, the FDA rules for factories that make medicine, food, cosmetics, and medical devices. And because the group plans to share its insulin-production framework online, crossing state lines, there may be other legal issues on the horizon. One solution might be to partner with other players in the health care system, like hospitals and pharmacies, which create custom versions of everything from acetaminophen to opioids in a process called compounding and navigate the demands of the U.S. system already. However, that's likely to make the final product more expensive.

Ultimately, it's not clear that the Open Insulin Project's real goal is to facilitate insulin minilabs across the U.S. The group intends to put the plan for their designer insulin-producing yeast online as soon as it's done, but only for "research purposes," says Di Franco. And without brewing facilities or the ability to check and purify the hormone, the plans themselves are a long way—scientifically and legally—from the point where anyone will be injecting homegrown insulin. Di Franco has offered up his own body as a proving ground once the lawyers sign off: "I'd be thrilled to be the first person to take the insulin," he says.

There's ample evidence that insulin doesn't need to be as expensive as it is in the U.S., even without DIY labs. Just across the border in Canada, a vial of insulin costs $30. In January 2020, Colorado became the first U.S. state to put a $100 cap on copays for insulin. Connecticut, Delaware, Illinois, Maine, Minnesota, New Hampshire, New Mexico, New York, Utah, Virginia, Washington, and West Virginia have followed suit.

"It's not hard to produce," says Peccoud. "It should not be more expensive than Tylenol. Insulin is just pure greed. And a failure of government." ◻

A NOVEL DELIVERY SYSTEM

RESEARCHERS AT MIT ARE DEVELOPING A TINY, SWALLOWABLE DEVICE THAT CAN AUTOMATICALLY INJECT INSULIN INTO THE STOMACH.

BY ALICE PARK

Needles aren't popular. For people with type 1 diabetes (and some with type 2 diabetes) that can be a problem, since treatment requires regular injections with insulin.

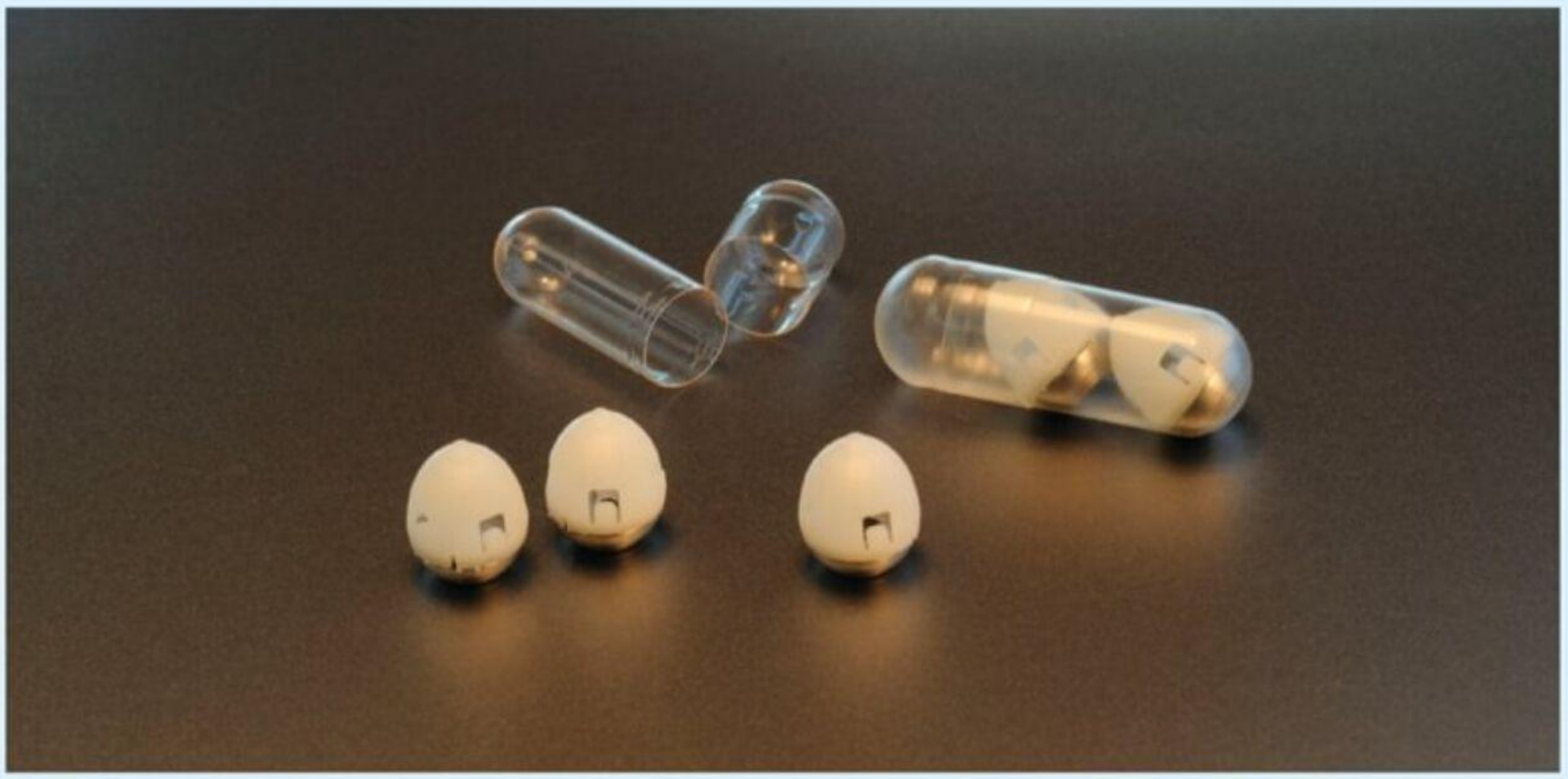
Recently, researchers at MIT came up with a novel way to eliminate the need for injections: a tiny swallowable device that can automatically inject insulin directly into the stomach wall. In a report published in *Science* in 2019, Robert Langer and Giovanni Traverso described what they called a self-orienting millimeter scale applicator, or SOMA, that they developed to make injecting drugs easier. To date, the device—roughly the size of a capsule and made of biodegradable materials—has only been tested in animals.

The SOMA is equipped with a spring-loaded needle that contains insulin. It's weighted so that it rights itself, and the opening for the needle will always find its mark (in this case, the stomach wall). When the team tested the SOMA in pigs, it consistently turned upright, with water in the stomach triggering a spring and the needle then piercing the stomach and delivering an insulin payload. In three pigs that swallowed the SOMA, the device led to similar insulin blood levels as injections through the skin.

Langer and Traverso said more studies need to be done in more animals, but they believe the technology has the potential to deliver a variety of drugs. Many people are still uncomfortable with the idea of injecting themselves with a needle, they said, and studies show that discomfort and fear has led to a seven- to eight-year delay in starting insulin treatment on average for people with diabetes. "We see tremendous potential in eventually treating many diseases," said Traverso.

The SOMA was inspired by the leopard tortoise, which has a uniquely narrowed shell that allows it to right itself after falling on its back. In addition, the design of the SOMA makes it possible for the device to inject properly even if the animal moves around after swallowing it.

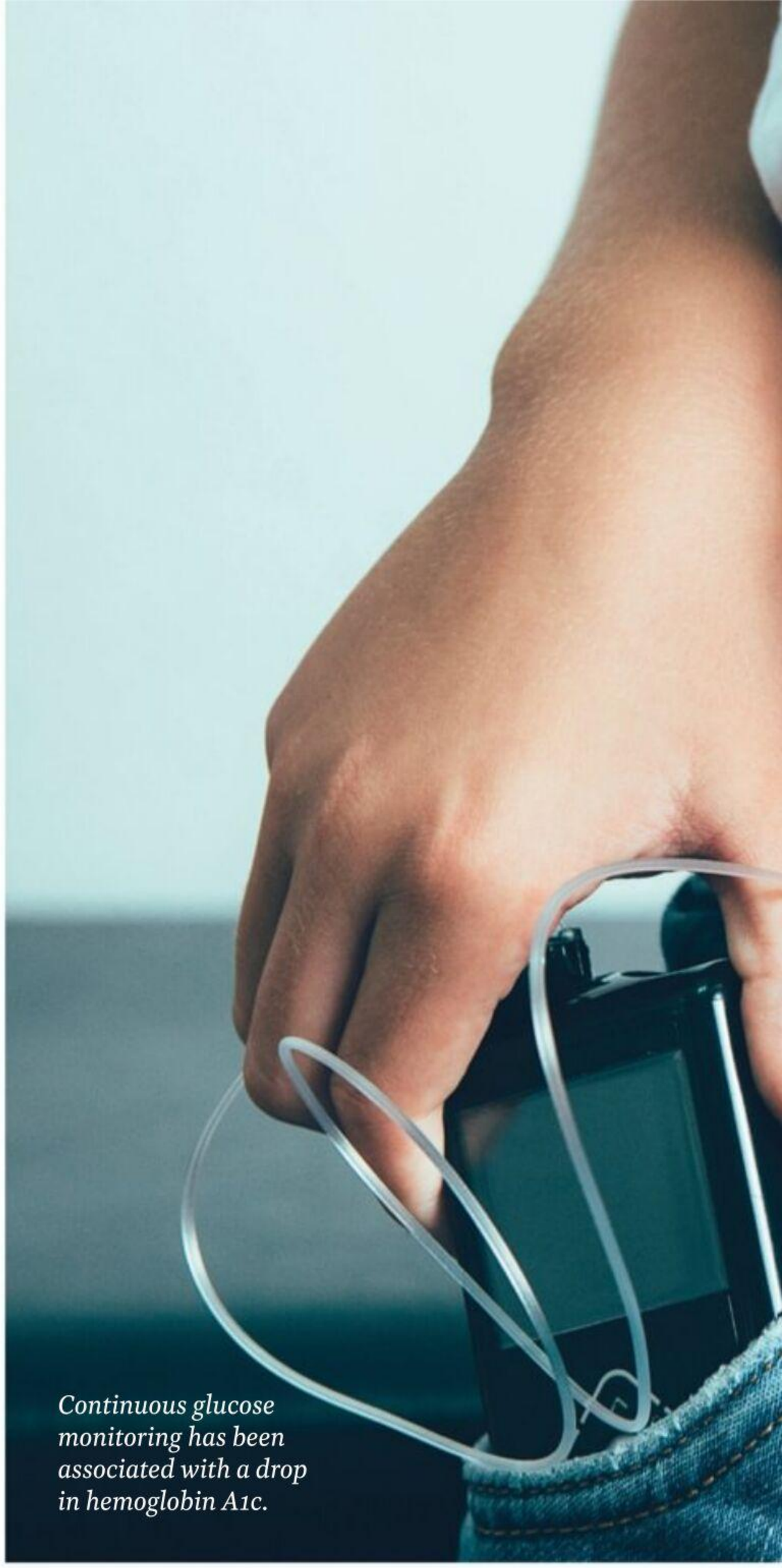
In order for the device to operate properly, the stomach must be empty, as food makes it harder for the SOMA to attach to the stomach wall. After the drug is delivered, the device is excreted. Langer and Traverso did not see any adverse effects from the device in the more than one dozen pigs that swallowed it.



ON THE HORIZON

FROM TECHNOLOGY TO PHARMACEUTICALS TO DIETS, NEW TREATMENTS AND A BETTER UNDERSTANDING OF DIABETES HAVE THE POTENTIAL TO CHANGE THE NARRATIVE AROUND THE DISEASE.

BY MARKHAM HEID



Continuous glucose monitoring has been associated with a drop in hemoglobin A1c.

EXPERTS OFTEN TALK ABOUT THE "burden" of a disease or illness. The word acts as a tidy container for the unpleasantness a person with a condition may experience—from symptoms to the cost of care to restrictions imposed on a person's lifestyle to health complications that may arise. For people with type 2 diabetes, this burden can be high.

Routine management of type 2 diabetes often involves major changes to one's diet and physical activity. For many, especially those taking insulin to manage their blood sugar, the disease can necessitate daily blood-glucose monitoring, a process that entails pricking a finger to draw blood and then dabbing that blood onto a glucose monitor test strip. Doing this several times a week—month after month—can present overlapping challenges. According to a 2013 survey in the journal *Diabetes Spectrum*, people find finger-prick glucose monitoring to be painful and tiresome, with results that can be confusing or unhelpful.

But with advancing drug therapies, such as the GLP-1 receptor agonists that mimic digestive hormones that act to suppress appetite, new high-tech devices to monitor blood-glucose levels, and advancements in bariatric surgery, the landscape for people with diabetes is improving. Here, experts describe some of the latest developments.

CONTINUOUS GLUCOSE MONITORS

People with type 1 diabetes typically have to check their blood-sugar levels daily or even multiple times each day. Because testing is such a big part of man-

aging the disease, research on continuous glucose monitors (CGMs)—devices as small as a quarter that use a small under-the-skin needle to monitor blood sugar levels—started with these patients.

Yet, more than 90 percent of people with diabetes have type 2 diabetes, roughly a third of whom are using insulin. This population was slow to adapt to CGMs but today has embraced the technology wholeheartedly, in part because research has pointed to significant benefits. For a study published in 2021 in the *Journal of the American Medical Association*, Dr. Roy Beck, medical director of the nonprofit Jaeb Center for Health Research, in Tampa, and his colleagues compared continuous glucose monitoring to standard finger-prick tests among people with type 2 diabetes who were using insulin. They found that continuous monitoring was associated with a significantly greater drop in hemoglobin A1c, the amount of glucose found in the blood. They also found that continuous monitoring helped people avoid risky and severe drops in blood sugar, or hypoglycemia. "It's pretty clear that there's a benefit for people with type 2 diabetes who are using insulin," Beck says.

Even for people with type 2 diabetes who are not taking insulin, continuous glucose monitoring could be helpful, says Beck. "There's a need for more studies to prove it, but it makes sense that it would likely have benefits," he says. For example, monitoring blood sugar in real time could help people make diet or lifestyle changes that reduce their risks for long-term health complications. "Normally, blood glucose following a meal shouldn't go above 140 milligrams per deciliter," he says.

Based on factors like diet, meal timing, and exercise habits, someone with type 2 diabetes may experience post-meal blood-sugar spikes that surpass 200 mg/dL or even 300 mg/dL. These spikes could cause few symptoms or short-term consequences, Beck says, but over time they can contribute to the development of common diabetes-related complications such as kidney failure, heart disease, or diabetic retinopathy (an eye condition that can cause blurry vision or blindness). "The first time people use these continuous monitors, it can be a real eye-opener," Beck adds. "I think they could be most helpful for self-management, and type 2 diabetes is a disease where self-management through diet and exercise can make a huge difference."

Other experts second this. "Patients using these devices can receive a graph of their glucose values over time, which helps them understand the effects of nutrition on glucose control, or how they could modify their exercise to make improvements," says Dr. Ilias Spanakis, an associate professor of medicine in the division of endocrinology, diabetes, and nutrition at the University of Maryland School of Medicine. In March 2024, the FDA approved the first over-the-counter continuous glucose monitor, which can be used by adults with or without diabetes who don't use insulin. Experts say the new device may be a good option for those with type 2 diabetes or prediabetes who want to better understand their glucose levels.

For a patient who relies on insulin to manage blood glucose, combining a continuous glucose monitor with an insulin pump could lead to major improvements. "Smart algorithms that connect the two can automatically adjust glucose based on glucose values," Spanakis says. This is already possible, and it's likely to become much more commonplace, he adds.

Monitoring blood sugar in real time could help people make diet or lifestyle changes that reduce the risk of health complications.

BARIATRIC SURGERY

Historically, bariatric (weight-loss) surgery has been used primarily to manage severe obesity, which the U.S. Centers for Disease Control and Prevention defines as having a body mass index (BMI) of 40 or higher. Many people who are severely obese also have diabetes, and research has found that bariatric surgery can help reduce the burden of type 2 diabetes or even send it into remission.

There are many different types of bariatric surgery, but one of the most common is the Roux-en-Y gastric bypass, in which the surgeon divides the stomach into two pouches. The small intestine is then directed to the smaller pouch, bypassing the larger portion of the stomach. This newly created pouch is typically only about the size of a walnut (while the stomach can normally hold roughly three pints of food), which means fewer calories will be ingested.

A 2018 study from researchers at the University of Oklahoma found that

Roux-en-Y gastric bypass surgery vastly outperformed typical medical management techniques, such as diet changes, doctor's visits, and prescription drugs, among people with type 2 diabetes. Surgery led to diabetes remission in roughly 28 percent of patients, compared with a remission rate of just 4 percent among the nonsurgery group, according to the study results.

"Surgery does not just lead to weight loss but also to an improvement in glycemic control, which happens even before the weight loss occurs," says Francisco Pasquel, associate professor of medicine at Emory University, who has published work on the benefits of bariatric surgery for people with type 2 diabetes. Exactly how the surgery does this isn't well understood, he says. However, bariatric surgery affects appetite, food intake, caloric absorption, and multiple neuroendocrine pathways—all of which could contribute to its beneficial actions for people with type 2 diabetes.

NEW PHARMACEUTICAL DRUGS

There are a lot of different diabetes drugs on the market, each with its own risks and benefits. But experts say two types are emerging as potential game changers when it comes to type 2 diabetes.

Glucagon-like peptide-1 (GLP-1) is a hormone released in the gut during digestion—one that plays a role in blood-sugar homeostasis. A class of drugs known as GLP-1 receptor agonists interact with GLP-1 receptors in ways that lower appetite, slow digestion, and provide other benefits for people with type 2 diabetes. These GLP-1 drugs aren't new. But Pasquel says the latest versions are different in that they work on two different receptors, not one. "Recent evidence shows that activating both receptors has a remarkable impact on weight loss and glycemic control," he says. For people with type 2 diabetes who are at high risk for heart disease or arterial disease, these new drugs seem to be a big upgrade over previous medications, says Pasquel.

A second category of drug has also emerged as a standout in the treatment of type 2 diabetes. Known as sodium-glucose cotransporter-2 (SGLT-2) inhibitors, these drugs help the kidneys remove sugar from a person's blood. Not only does this improve blood-sugar control in people with type 2 diabetes, it also helps protect them from heart failure and kidney disease. Pasquel says these drugs are so effective that they're now being used by people with heart failure or kidney disease who do not have type 2 diabetes.

EMERGING WAYS TO THINK ABOUT WEIGHT LOSS

Experts have long understood that weight loss can help reduce type 2 diabetes symptoms and risks. This recognition has led to research on a number of weight-loss diets. More research is needed, but some of the latest studies suggest that fasting plans—in particular, intermittent fasting—may be particularly beneficial for people with type 2 diabetes.

Intermittent fasting involves cutting out calorie-containing food and drinks for an extended period of time—anywhere from 12 hours to two days, depending on the approach a person chooses. A 2019 research review in the journal *Nutrients* found that intermittent fasting promotes weight loss, increases insulin sensitivity, and reduces insulin levels in the blood. All of this is helpful for people with type 2 diabetes. "Essentially, fasting is doing what we prescribe diabetes medications to do, which is to improve insulin sensitivity," says Benjamin Horne, director of cardiovascular and genetic epidemiology at Intermountain Healthcare, in Utah.

MORE RESEARCH IS NEEDED, BUT SOME OF THE LATEST STUDIES SUGGEST THAT FASTING PLANS—SUCH AS INTERMITTENT FASTING—MAY BE BENEFICIAL FOR PEOPLE WITH TYPE 2 DIABETES.

It's not yet clear which form of intermittent fasting is best in regards to type 2 diabetes. But Horne says that time-restricted eating—a type of fasting that involves consuming the day's calories during a single six- or eight-hour feeding window—is leading the pack, largely because patients are able to stick with it.

The interventions described here are some of the most promising, but they have company. It's safe to say that, looking ahead, more people with type 2 diabetes will be able to effectively manage or mitigate their symptoms. ☐

VIRTA HEALTH

AN ONLINE PLATFORM SEEKS TO COUNSEL PEOPLE WITH TYPE 2 DIABETES TO ACHIEVE REMISSION THROUGH DIET AND HEALTH COACHING.

BY ANGELA HAUPT

Type 2 diabetes care has long centered on management with medication. Telemedicine provider Virta Health aims to flip that paradigm to focus on diabetes reversal through personalized nutrition and health coaching.

The company is the brainchild of Sami Inkinen (founder of real estate start-up Trulia) a fitness enthusiast and Ironman competitor who discovered he was prediabetic in 2014. Following the diagnosis, Inkinen partnered with two experts in metabolic health and launched Virta, a remote-care platform that uses a ketogenic diet intervention (low-carbohydrate, fat-rich) paired with education, coaching, and physician management of medications, in order to improve the health of those with type 2 diabetes. The platform states that the program potentially may help with weight loss as well.

In a study published in *Diabetes Therapy* (a peer-reviewed, rapid-publication journal) participants in a Virta Health clinical trial eliminated 63 percent of their diabetes-specific medications, and 94 percent reduced or eliminated insulin use. "Traditional disease management for chronic diseases hasn't worked. It's largely pharmaceutical-based," Virta president Kevin Kumler says of his product. (Standard diabetes care also includes diet and exercise, not just medication.)

Recently, Virta has partnered with a number of health-insurance plans, including Humana and Banner/Aetna, making it more widely available.

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CALCULATING THE IMPACT

BY AVA ERICKSON

38 MILLION

U.S. ADULTS WITH DIABETES.

ONE IN FIVE

Estimated number of Americans who have prediabetes and don't know it.

$35: THE MAX MONTHLY CO-PAY FOR INSULIN FROM THE THREE MAJOR INSULIN MANUFACTURERS IN THE U.S.

675

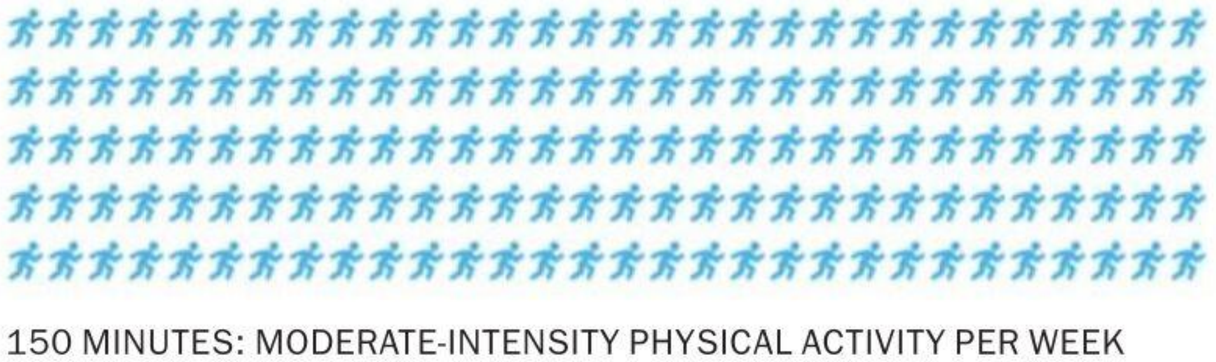
PREDICTED PERCENT INCREASE BY 2060 OF PEOPLE UNDER THE AGE OF 20 WHO WILL HAVE TYPE 2 DIABETES.

$413 BILLION

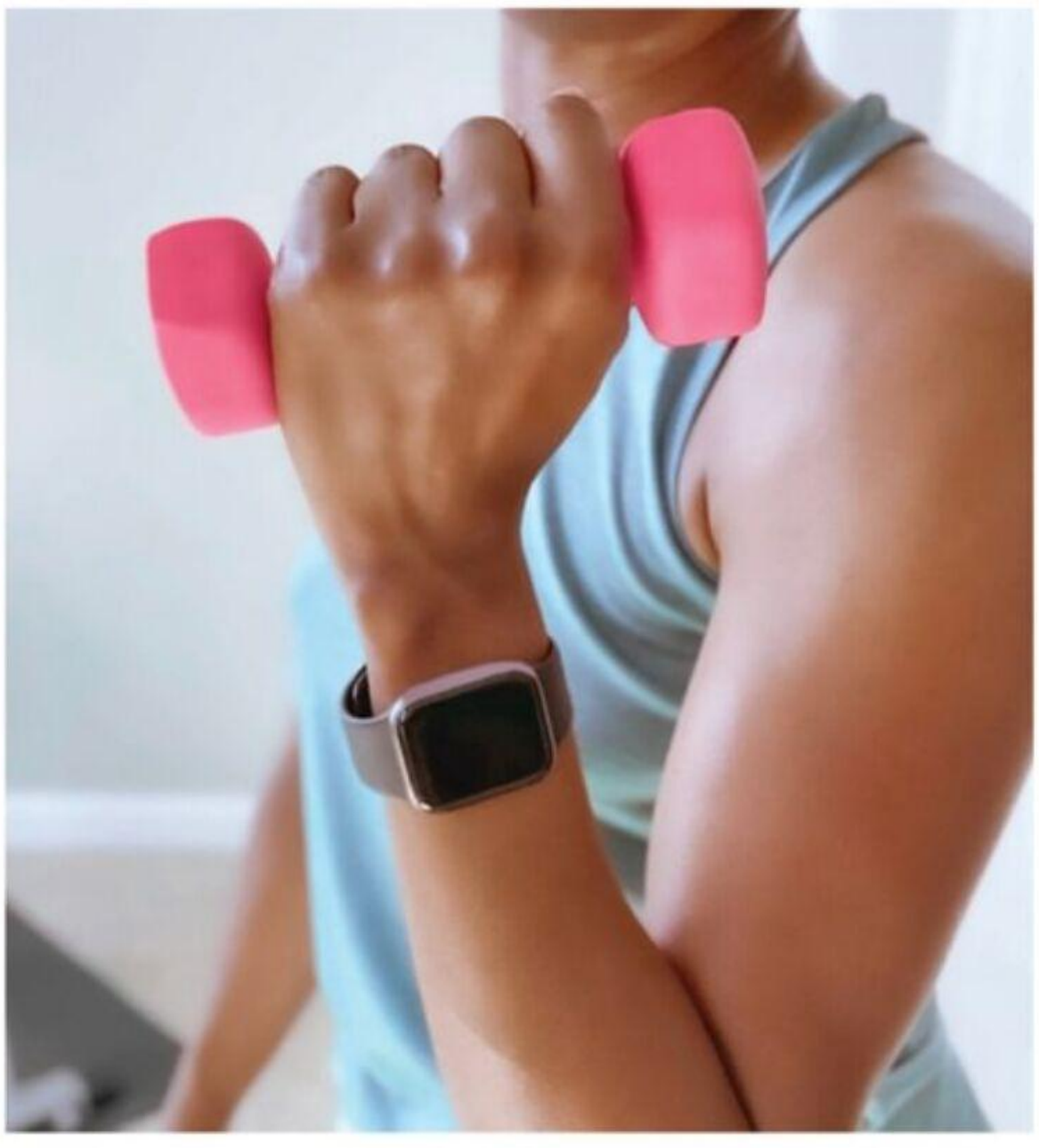
The total estimated cost of diagnosed diabetes in 2022.

30-40%

THE INCREASE IN RISK OF DIABETES FOR SMOKERS.



150 MINUTES: MODERATE-INTENSITY PHYSICAL ACTIVITY PER WEEK RECOMMENDED BY THE CDC TO PREVENT DIABETES.

Solutions, Strategies, Success

More Americans have diabetes than ever, but medical science's ability to treat the condition is improving all the time. Along with GLP-1 drugs and the latest glucose monitors, new treatments and greater understanding of the disease are helping millions live their lives to the fullest.